MOLECULES FOR INDUCING DIFFERENTIATION OF DENDRITIC CELLS

RELATED APPLICATIONS

This application claims priority to U.S. Provisional Patent Application No. 60/512,183, filed October 20, 2003, whose contents are incorporated by reference. This application is also related to U.S. Application No. _____, filed December 30, 2003, entitled "Method and Composition for Treating Osteoporosis". This application is also related to U.S. Application No. _____, filed December 31, 2003, entitled "Method of Inducing Differentiation of Dendritic Cells".

FIELD OF INVENTION:

The present invention relates to compounds general formula Z-OC (C $R_{n1}R_{n2}$) -CO-Z wherein Z = OH or NH_2 and n1 = n2 =1 to 8, for modulation of immune response by differentiation of dendritic cells containing novel class of amino acid / dicarboxylic acid derivatives of the general formula ZOC-CR_3R_4-CR_1R_2-COOH, ZOC-CR_5R_6-CR_3R_4-CR_1R_2-COOH, ZOC-CR_7R_8-CR_5R_6-CR_3R_4-CR_1R_2-COOH.

BACKGROUND AND PRIOR ART REFERENCES:

Indian green mussels (*Perna viridis*) are the cheap source of proteins and considered as a delicacy. Extract prepared from green mussels by enzyme-acid hydrolysis process showed various biological activities. In our earlier patent (US patent application #20030044470) we have shown the inhibition of osteoclast differentiation and activation in the crude extract. In same continuation, attempts have been made to purify the active compound that showed inhibition of osteoclast differentiation and activation. The purification of the crude extract was done using HPLC, gel filtration and TLC methods. The purified compound was again checked for the above activity. The compound was characterized using NMR and LC-MS/MS techniques. This compound was synthesized and checked for the presence of the above biological activity. This patent in particular describes the synthesis of the compound and also its activity for inhibition of osteoclast formation.

Novel class of amino acid/dicarboxylic acid derivatives (sulfonic acid / sulfate derivatives of naturally occurring amino acids and their amides) along with calcium is for their activation to show inhibition of the dendritic cells. Amino acid derivatives and calcium ion when used separately did not show any activity on differentiation of dendritic cells. The following classes of compounds are identified.

(1) Natural acidic amino acids (Aspartic acid, Glutamic acid and their amides),

(2) Unnatural amino acids, amides such as homoglutamic acid,

(3) Dicarboxylic acids such as succinic acid, glutaric acid, and adipic acid

(4) N-sulfonyl, C-sulfonyl / sulfate derivatives of the above acids

(5) Alkali and alkaline earth metals such as Na, K, Mg, Zn and Ca as their suitable salts

A number of molecules are known to induce the differentiation and maturation of dendritic cells from precursors. Some of the recent ones are listed below:

1. The most studied is differentiation of DCs with GM-CSF which is the conventional method to generate DCs from bone marrow. The DCs obtained in this manner are immature in nature.
2. Maturation of DCs is normally obtained by stimulating the immature DCs with Tumor Necrosis Factor-alpha (TNF-□). Recently TNF-□ has been shown to induce the differentiation of DCs from monocytes.
3. CD40 ligand (CD40l) that is normally expressed on T cells also induces the maturation of DCs. An alternative for CD40l is the use of commercially available anti-CD40 monoclonal antibody.
4. Stimulation with the extracellular endotoxin, Lipopolysaccharide (LPS) from *Escherichia coli* is also a common method to mature DCs
5. Atrial natriuretic peptide (ANP) a cardiovascular hormone secreted mainly by the cardiac atria regulates the volume-pressure homeostasis. The action of ANP is mediated by its receptor, guanylyl cyclase-coupled receptor A (GC-A) and has recently been shown to induce the maturation of DCs by increasing cytokine secretion and increases in various cell surface molecule expression.

6. The imidazoquinoline compounds imiquimod and R-848 are low-molecular-weight anti-viral compounds that are immune response modifiers and induce the synthesis of interferon-alpha and other cytokines in a variety of cell types. These compounds have potent anti-viral and anti-tumor properties and have recently been shown to induce the activation of macrophages and splenocytes and induce the maturation of Dendritic cells.
7. Stimulation of Flt3 receptor tyrosine kinase through its cognate ligand expands early hematopoietic progenitor and Dendritic cells (DCs) in humans and mice.
8. Prostaglandin E2, found at high concentrations under the skin has been shown to facilitate initiation of skin immune responses by promoting the migration and maturation of Langerhans cells, a DC subtype found under the epidermis and in the dermis of the skin.
9. Fermented mistletoe extract often used for adjuvant treatment of cancer patients, significantly stimulated the maturation of pre-differentiated immature DC, as evidenced by a heightened expression of CD83. Like the positive control TNF-alpha, the mistletoe extract significantly activated CD80 and CD86 as well as HLA class I and II molecules on these cells.
10. Lysophosphatidylcholine (LPC) is a major lipid component of oxidized low density lipoprotein with reported pro-inflammatory activities. It is now reported that LPC acts through G protein-coupled receptors on differentiating monocytes to generate mature dendritic cells with the ability to stimulate IL-2 and IFN-gamma production by allogeneic T lymphocytes.

OBJECTIVE OF INVENTION

The objective of the invention relates to compounds compounds general formula Z-OC (C $R_{n1}R_{n2}$) -CO-Z wherein Z = OH or NH_2 and n1 = n2 =1 to 8. for modulation of immune response by differentiation dendritic cells containing novel class of amino acid / dicarboxylic acid derivatives (sulfonic acid / sulfate derivatives of naturally occurring amino acids and their amides).: Compounds for induction of differentiation of dendritic cells containing novel class of amino acid / dicarboxylic acid derivatives of the general formula ZOC-CR_3R_4-CR_1R_2-COOH, ZOC-CR_5R_6-CR_3R_4-CR_1R_2-COOH, ZOC-CR_7R_8-

CR_5R_6-CR_3R_4-CR_1R_2-COOH wherein Z= OH or NH_2; R_1, to R_8 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$. wherein all the symbols are the same meaning as hereinafter defined and non-toxic salts thereof as an active ingredient.

Another objective of the present invention relates to a method for modulation of immune response controlled by differentiating dendricts cells.

Another objective of the present invention relates to use of compound in vaccine formulation or in protection based studies to promote more efficient and faster presentation of the antigens to T-cell thereby initiative primary protective Th1 immune response and help in clearance in pathogens.

Another objective of the present invention relates to novel compound useful in vaccination, cancer therapy and other immunomodulatory regiments.

The further objective of the present invention relates to administration a pharmaceutical acceptable amount of a compound optionally with an additive, excipient, diluents or carrier for modulation of immune response.

SUMMARY OF THE INVENTION

This invention is related to compounds compounds general formula Z-OC (C $R_{n1}R_{n2}$) -CO-Z wherein Z = OH or NH_2 and n1 = n2 =1 to 8. for modulation of immune response by differentiation for induction of differentiation of dendritic cells containing novel class of amino acid / dicarboxylic acid derivatives (sulfonic acid / sulfate derivatives of naturally occurring amino acids and their amides). More particularly, this invention is related to:

1) Compounds for induction of differentiation of dendritic cells containing novel class of amino acid / dicarboxylic acid derivatives of the general formula ZOC-CR_3R_4-CR_1R_2-COOH, ZOC-CR_5R_6-CR_3R_4-CR_1R_2-COOH, ZOC-CR_7R_8-CR_5R_6-CR_3R_4-CR_1R_2-COOH wherein Z= OH or NH_2; R_1, to R_8 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$.
   wherein all the symbols are the same meaning as hereinafter defined and non-toxic salts thereof as an active ingredient,
2) The compounds inducing differentiation of dendritic cells also contain different divalent metal cations such as Mg, Ca and Zn,

wherein all the symbols are the same meaning as hereinafter defined and non-toxic salts thereof as an active ingredient,

3) The composition consists of varying amounts of the above amino acid/ dicarboxylic acid derivatives and their pharmaceutically acceptable selected alkali / alkaline earth metal salts,

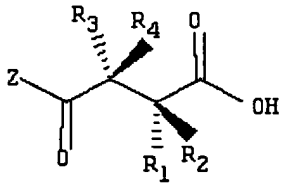
wherein all the symbols are the same meaning as hereinafter defined and non-toxic salts thereof as an active ingredient,

4) The process for the preparation of the aforesaid compounds, useful in inducing differentiation of dendritic cells.

DETAILED DESCRIPTION OF THE INVENTION

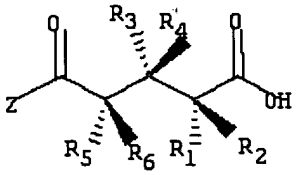
The present invention is relates to a compound of general formula Z-OC (C $R_{n1}R_{n2}$) -CO-Z wherein Z = OH or NH_2 and n1 = n2 =1 to 8.

Yet another embodiments of a present invention relates to a compound having a structure as shown below and bearing general formula ZOC-CR_3R_4-CR_1R_2-COOH wherein:Z=OH or NH_2, R_1, to R_4 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$



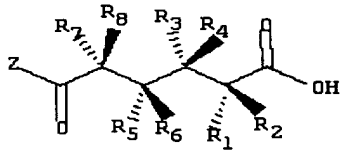
Structure 1

Yet another embodiments of a present invention relates to a compound having a structure as shown below and bearing general formula ZOC- CR_5R_6-CR_3R_4-CR_1R_2-COOH wherein: Z=OH or NH_2, R_1 to R_6 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$



Structure 2

Yet another embodiments of a present invention relates to a compound having a structure as shown below and bearing general formula ZOC-CR_7R_8-CR_5R_6-CR_3R_4-CR_1R_2-COOH wherein: Z=OH or NH_2, R_1 to R_8 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$



structure 3

Yet another embodiments of a present invention relates to a compound formula (Ia), wherein the compound is selected from the group consisting of:

I. [L- Aspartic acid, N-Sulfonic acid],
II. [2α,3-dicarboxy, propane-1-sulfonic acid],
III. [2α,3-dicarboxy, propane-1-sulfate],
IV. [1α,2-carboxy ethane sulfonic acid],
V. [1α,2-carboxy ethane sulfate],
VI. [D-aspartic acid, N-sulfonic acid],
VII. [2β,3-carboxy,propane-1-sulfonic acid],
VIII. [2β,3-carboxy,propane-1-sulfate],
IX. [1β,2-carboxy ethane-1-sulfonic acid],
X. [1β,2-carboxy ethane-1-sulfate],

XI. [D-aspartic acid, 3α -sulfonic acid],

XII. [D-aspartic acid, 3α-sulfate],

XIII. [D-aspartic acid, 3β-sulfonic acid],

XIV. [D-aspartic acid, 3β-sulfate],

XV. [L-asparagine,N-sulfonic acid],

XVI. [2α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVII. [2α-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1α-carboxy, 2-carboxamido, ethane sulfonic acid],

XIX. [1α-carboxy, 2-carboxamido, ethane sulfate],

XX. [L-asparagine, 3α-sulfonic acid],

XXI. [L-asparagine, 3α-sulfate],

XXII. [L-asparagine, 3β-sulfonic acid],

XXIII. [L-asparagine, 3β-sulfate,

XXIV. [D-asparagine, N-sulfonic acid],

XXV. [2β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXVI. [2β-carboxy, 3-carboxamido, propane-1-sulfate],

XXVII. [1β-carboxy, 2-carboxamido, ethane sulfonic acid],

XXVIII. [1β-carboxy, 2-carboxamido, ethane sulfate],

XXIX. [D-asparagine, 3α-sulfonic acid],

XXX. [D-asparagine, 3α-sulfate],

XXXI. [D-asparagine, 3β-sulfonic acid],

XXXII. [D-asparagine, 3β-sulfate],

XXXIII. [L-glutamic acid, N-sulfonic acid],

XXXIV. [2α,4-dicarboxy, butane-1-sulfonic acid],

XXXV. [2α, 4-dicarboxy, butane-1-sulfate],

XXXVI. [1α, 3-dicarboxy, propane sulfonic acid],

XXXVII. [1α, 3-dicarboxy, propane sulfate],

XXXVIII. [1β, 3-dicarboxy, propane sulfate],

XXXIX. [1β, 3-dicarboxy, propane sulfonic acid],

Yet another embodiment of a present invention relates to a compound formula (Ib) wherein the compound is selected from the group consisting of:

I. [D-glutamic acid, N-sulfonic acid],
II. [2β, 4-dicarboxy, butane-1-sulfonic acid],
III. [2β, 4-dicarboxy, butane-1-sulfate],
IV. [D-glutamic acid, 3α-sulfonic acid],
V. [D-glutamic acid, 3α-sulfate],
VI. [D-glutamic acid, 3β-sulfonic acid],
VII. [D-glutamic acid, 3β-sulfate],
VIII. [D-glutamic acid, 4α-sulfonic acid],
IX. [D-glutamic acid, 4α-sulfate],
X. [D-glutamic acid, 4β-sulfonic acid],
XI. [D-glutamic acid, 3β-sulfate],
XII. [L-glutamine, N-sulfonic acid],
XIII. [2α-carboxy, 4-carboxamido, butane-1-sulfonic acid],
XIV. [2α-carboxy, 4-carboxamido, butane-1-sulfate],
XV. [1α-carboxy, 3-carboxamido, propane-1-sulfonic acid],
XVI. [1α-carboxy, 3-carboxamido, propane-1-sulfate],
XVII. [1β-carboxy, 3-carboxamido, propane-1-sulfate],
XVIII. [1β-carboxy, 3-carboxamido, propane-1-sulfonic acid],
XIX. [D-glutamine, N-sulfonic acid],
XX. [2β-carboxy, 4-carboxamido, butane-1-sulfonic acid],
XXI. [2β-carboxy, 4-carboxamido, butane-1-sulfate],
XXII. [D-glutamine, 3α-sulfonic acid],
XXIII. [D-glutamine, 3α-sulfate],
XXIV. [D-glutamine, 3β-sulfonic acid],
XXV. [D-glutamine, 3β-sulfate],
XXVI. [D-glutamine, 4α-sulfonic acid],
XXVII. [D-glutamine, 4α-sulfate],
XXVIII. [D-glutamine, 4β-sulfonic acid],

XXIX. [D-glutamine, 4β-sulfate],

XXX. [L-homoglutamic acid, N-sulfonic acid],

XXXI. [Pentane-2α, 5-dicarboxy-1-sulfonic acid],

XXXII. [Pentane-2α, 5-dicarboxy-1-sulfate],

XXXIII. [Butane-1α, 4-dicarboxy-1-sulfonic acid],

XXXIV. [Butane-1α, 4-dicarboxy-1-sulfate],

XXXV. [D-homoglutamic acid, N-sulfonic acid],

XXXVI. [Pentane-2β, 5-dicarboxy-1-sulfonic acid],

XXXVII. [Pentane-2β, 5-dicarboxy-1-sulfate],

XXXVIII. [Butane-1β, 4-dicarboxy-1-sulfonic acid],

XXXIX. [Butane-1β, 4-dicarboxy-1-sulfate],

Yet another embodiment of a present invention relates to a compound formula (Ic) wherein the compound is selected from the group consisting of

I. [D-homoglutamic acid, 3α-sulfonic acid],

II. [D-homoglutamic acid, 3α-sulfate],

III. [D-homoglutamic acid, 3β-sulfonic acid],

IV. [D-homoglutamic acid, 3β-sulfate],

V. [D-homoglutamic acid, 4α-sulfonic acid],

VI. [D-homoglutamic acid, 4α-sulfate],

VII. [D-homoglutamic acid, 4β-sulfonic acid],

VIII. [D-homoglutamic acid, 4β-sulfate],

IX. [D-homoglutamic acid, 5α-sulfate],

X. [D-homoglutamic acid, 5α-sulfate],

XI. [D-homoglutamic acid, 5β-sulfonic acid],

XII. [D-homoglutamic acid, 5β-sulfate],

XIII. [L-homoglutamine, N-sulfonic acid],

XIV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfonic acid],

XV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfate],

XVI. [Butane-1α-carboxy, 4-carboxamido-1-sulfonic acid],

XVII. [Butane-1α-carboxy, 4-carboxamido-1-sulfate],

XVIII. [D-homoglutamine, N-sulfonic acid],

XIX. [Pentane-2β-carboxy, 5-carboxamido-1-sulfonic acid],

XX. [Butane-1 β -carboxy, 4-carboxamido-1-sulfonic acid],

XXI. [Butane-1 β -carboxy, 4-carboxamido-1-sulfate],

XXII. [D-homoglutamine, 3α-sulfonic acid],

XXIII. [D-homoglutamine, 3α-sulfate],

XXIV. [D-homoglutamine, 3β-sulfonic acid],

XXV. [D-homoglutamine, 3β-sulfate],

XXVI. [D-homoglutamine, 4α-sulfonic acid],

XXVII. [D-homoglutamine, 4α-sulfate],

XXVIII. [D-homoglutamine, 4β-sulfonic acid],

XXIX. [D-homoglutamine, 4β-sulfate],

XXX. [D-homoglutamine, 5α-sulfonic acid],

XXXI. [D-homoglutamine, 5α-sulfate],

XXXII. [D-homoglutamine, 5β-sulfonic acid] and

XXXIII. [D-homoglutamine, 5β-sulfate].

Yet another embodiment of a present invention relates to a compound Novel sulfonic acid / sulfate derivatives of the formulae $ZOC\text{-}CR_3R_4\text{-}CR_1R_2\text{-}COOH$ wherein: Z=OH or NH_2, R_1, to R_4 denotes H, NH_2, SO_3H, or OSO_3H, $CH_2\text{-}SO_3H$, $CH_2\text{-}OSO_3H$, $NHSO_3H$

I. A compound wherein Z=OH, $R_2=R_3=R_4=H$, $R_1= NHSO_3H$ is the same meaning as is before defined;

II. A compound wherein Z=OH, $R_2=R_3=R_4=H$, $R_1= CH_2SO_3H$ is the same meaning as is before defined;

III. A compound wherein Z=OH, $R_2=R_3=R_4=H$, $R_1= CH_2OSO_3H$ is the same meaning as is before defined;

IV. A compound wherein Z=OH, $R_2=R_3=R_4=H$, $R_1=SO_3H$ is the same meaning as is before defined;

V. A compound wherein Z=OH, $R_2=R_3=R_4=H$, $R_1=OSO_3H$ is the same meaning as is before defined;

VI. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2= $NHSO_3H$ is the same meaning as is before defined;

VII. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2= CH_2SO_3H is the same meaning as is before defined;

VIII. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2= CH_2OSO_3H is the same meaning as is before defined;

IX. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2=SO_3H is the same meaning as is before defined;

X. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2=OSO_3H is the same meaning as is before defined;

XI. A compound wherein Z=OH, R_1=R_4=H, R_2=NH_2, R_3=SO_3H is the same meaning as is before defined;

XII. A compound wherein Z=OH, R_1=R_4=H, R_2=NH_2, R_3=SO_3H is the same meaning as is before defined;

XIII. A compound wherein Z=OH, R_1=R_3=H, R_2=NH_2, R_4=SO_3H is the same meaning as is before defined;

XIV. A compound wherein Z=OH, R_1=R_3=H, R_2=NH_2, R_4=OSO_3H is the same meaning as is before defined;

XV. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1=$NHSO_3H$ is the same meaning as is before defined;

XVI. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1=CH_2SO_3H is the same meaning as is before defined;

XVII. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1= CH_2OSO_3H is the same meaning as is before defined;

XVIII. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1=SO_3H is the same meaning as is wherein Z=NH_2, R_2=R_3=R_4=H, R_1=OSO_3H is the same meaning as is before defined;

XIX. A compound wherein Z=NH_2, R_1=R_4=H, R_2=NH_2, R_3= SO_3H is the same meaning as is before defined;

XX. A compound wherein $Z=NH_2$, $R_1=R_4=H$, $R_2=NH_2$, $R_3= OSO_3H$ is the same meaning as is before defined;

XXI. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2=NH_2$, $R_4= SO_3H$ is the same meaning as is before defined;

XXII. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2= NH_2$, $R_4= OSO_3H$ is the same meaning as is before defined;

XXIII. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2= NHSO_3H$ is the same meaning as is before defined;

XXIV. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2= CH_2SO_3H$ is the same meaning as is before defined;

XXV. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2= CH_2OSO_3H$ is the same meaning as is before defined;

XXVI. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2=SO_3H$ is the same meaning as is before defined;

XXVII. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2=OSO_3H$ is the same meaning as is before defined;

XXVIII. A compound wherein $Z=NH_2$, $R_1=R_4=H$, $R_2=NH_2$, $R_3= SO_3H$ is the same meaning as is before defined;

XXIX. A compound wherein $Z=NH_2$, $R_1=R_4=H$, $R_2=NH_2$, $R_3= OSO_3H$ is the same meaning as is before defined;

XXX. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2=NH_2$, $R_4=SO_3H$ is the same meaning as is before defined;

XXXI. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2=NH_2$, $R_4=OSO_3H$ is the same meaning as is before defined.

Yet another embodiment of a present invention relates to a compound novel sulfonic acid / sulfate derivatives of the formulae $ZOC-CR_5R_6-CR_3R_4-CR_1R_2-COOH$, wherein: Z=OH or NH_2, R_1, to R_6 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, $CH_2-\ OSO_3H$, $NHSO_3H$

I. A compound wherein Z=OH, $R_2=R_3=R_4=R_5=R_6=H$, $R_1=NHSO_3H$ is the same meaning as is before defined;

II. A compound wherein Z=OH, R_2=R_3=R_4=R_5=R_6=H, R_1= CH_2SO_3H is the same meaning as is before defined;

III. A compound wherein Z=OH, R_2=R_3=R_4=R_5=R_6=H, R_1=CH_2OSO_3H is the same meaning as is before defined;

IV. A compound wherein Z=OH, R_2=R_3=R_4= R_5=R_6=H, R_1= SO_3H is the same meaning as is before defined;

V. A compound wherein Z=OH, R_2=R_3=R_4=R_5=R_6=H, R_1=OSO_3H is the same meaning as is before defined;

VI. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6=H, R_2=OSO_3H is the same meaning as is before defined;

VII. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6=H, R_2= SO_3H is the same meaning as is before defined;

VIII. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6=H, R_2= $NHSO_3H$ is the same meaning as is before defined;

IX. A compound wherein Z=OH, R_1=R_3=R_4= R_5=R_6=H, R_2= CH_2SO_3H is the same meaning as is before defined;

X. A compound wherein Z=OH, R_1=R_3=R_4= R_5=R_6=H, R_2= CH_2OSO_3H is the same meaning as is before defined;

XI. A compound wherein Z=OH, R_1=R_4=R_5=R_6=H, R_2= NH_2, R_3=SO_3H is the same meaning as is before defined;

XII. A compound wherein Z=OH, R_1=R_4=R_5=R_6=H, R_2= NH_2, R_3=OSO_3H is the same meaning as is before defined;

XIII. A compound wherein Z=OH, R_1=R_3=R_5=R_6=H, R_2= NH_2, R_4= SO_3H is the same meaning as is before defined;

XIV. A compound wherein Z=OH, R_1=R_3=R_5=R_6=H, R_2= NH_2, R_4=OSO_3H is the same meaning as is before defined;

XV. A compound wherein Z=OH, R_1=R_4= R_3=R_6=H, R_2= NH_2, R_5=SO_3H is the same meaning as is before defined;

XVI. A compound wherein Z=OH, R_1=R_4=R_3=R_6=H, R_2= NH_2, R_5=OSO_3H is the same meaning as is before defined;

XVII. A compound wherein Z=OH, R_1=R_3=R_5=R_4=H, R_2= NH_2, R_6=SO_3H is the same meaning as is before defined;

XVIII. A compound wherein Z=OH, R_1=R_3=R_5=R_4=H, R_2= NH_2, R_6=OSO_3H is the same meaning as is before defined;

XIX. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1=$NHSO_3H$ is the same meaning as is before defined;

XX. A compound wherein Z=NH_2, R_2=R_3=R_4= R_5=R_6=H, R_1=CH_2SO_3H is the same meaning as is before defined;

XXI. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1= CH_2OSO_3H is the same meaning as is before defined;

XXII. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1=SO_3H is the same meaning as is before defined;

XXIII. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1= OSO_3H is the same meaning as is before defined;

XXIV. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= OSO_3H is the same meaning as is before defined;

XXV. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= SO_3H is the same meaning as is before defined;

XXVI. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= $NHSO_3H$ is the same meaning as is before defined;

XXVII. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2=CH_2SO_3H is the same meaning as is before defined;

XXVIII. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= CH_2OSO_3H is the same meaning as is before defined;

XXIX. A compound wherein Z=NH_2, R_1=R_4=R_5=R_6=H, R_2= NH_2, R_3=SO_3H is the same meaning as is before defined;

XXX. A compound wherein Z=NH_2, R_1=R_4=R_5=R_6=H, R_2= NH_2, R_3=OSO_3H is the same meaning as is before defined;

XXXI. A compound wherein Z=NH_2, R_1=R_3=R_5=R_6=H, R_2= NH_2, R_4=SO_3H is the same meaning as is before defined;

XXXII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_6=H$, $R_2= NH_2$, $R_4=OSO_3H$ is the same meaning as is before defined;

XXXIII. A compound, wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=H$, $R_2= NH_2$, $R_5=SO_3H$ is the same meaning as is before defined;

XXXIV. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=H$, $R_2= NH_2$, $R_5=OSO_3H$ is the same meaning as is before defined;

XXXV. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=H$, $R_2= NH_2$, $R_6=SO_3H$ is the same meaning as is before defined;

XXXVI. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=H$, $R_2= NH_2$, $R_6=OSO_3H$ is the same meaning as is before defined.

Yet another embodiment of a present invention relates to a compound Novel sulfonic acid / sulfate derivatives of the formulae $ZOC\text{-}CR_7R_8\text{-}CR_5R_6\text{-}CR_3R_4\text{-}CR_1R_2\text{-}COOH$ as claimed in claim 4, wherein: Z=OH or NH_2, R_1, to R_8 denotes H, NH_2, SO_3H, or OSO_3H, $CH_2\text{-}SO_3H$, $CH_2\text{-}OSO_3H$, $NHSO_3H$

I. A compound wherein Z=OH, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1=NHSO_3H$ is the same meaning as is before defined;

II. A compound wherein Z=OH, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1= -CH_2SO_3H$ is the same meaning as is before defined;

III. A compound wherein Z=OH, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1=CH_2OSO_3H$ is the same meaning as is before defined;

IV. A compound wherein Z=OH, $R_2=R_3=R_4= R_5=R_6=R_7=R_8=H$, $R_1=SO_3H$ is the same meaning as is before defined;

V. A compound wherein Z=OH, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1=OSO_3H$ is the same meaning as is before defined;

VI. A compound wherein Z=OH, $R_1=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_2=NHSO_3H$ is the same meaning as is before defined;

VII. A compound wherein Z=OH, $R_1=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_2=CH_2SO_3H$ is the same meaning as is before defined;

VIII. A compound wherein Z=OH, $R_1=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_2=CH_2OSO_3H$ is the same meaning as is before defined;

IX. A compound wherein Z=OH, R_1=R_3=R_4= R_5=R_6=R_7=R_8=H, R_2=SO_3H is the same meaning as is before defined;

X. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6= R_7=R_8=H, R_2=OSO_3H is the same meaning as is before defined;

XI. A compound wherein Z=OH, R_1=R_4= R_5=R_6= R_7=R_8=H, R_2=NH_2, R_3=SO_3H is the same meaning as is before defined;

XII. A compound wherein Z=OH, R_1=R_4=R_5=R_6=R_7=R_8=H, R_2=NH_2, R_3=OSO_3H is the same meaning as is before defined;

XIII. A compound wherein Z=OH, R_1=R_3=R_5=R_6= R_7=R_8=H, R_2= NH_2, R_4=SO_3H is the same meaning as is before defined;

XIV. A compound wherein Z=OH, R_1=R_3=R_5=R_6=R_7=R_8=H, R_2=NH_2, R_4=OSO_3H is the same meaning as is before defined;

XV. A compound wherein Z=OH, R_1=R_4= R_3=R_6= R_7=R_8=H, R_2=NH_2, R_5=SO_3H is the same meaning as is before defined;

XVI. A compound wherein Z=OH, R_1=R_4=R_3=R_6= R_7=R_8=H, R_2=NH_2, R_5=OSO_3H is the same meaning as is before defined;

XVII. A compound wherein Z=OH, R_1=R_3=R_5=R_4= R_7=R_8=H, R_2=NH_2, R_6=SO_3H is the same meaning as is before defined;

XVIII. A compound wherein Z=OH, R_1=R_3=R_5=R_4= R_7=R_8=H, R_2=NH_2, R_6=OSO_3H is the same meaning as is before defined;

XIX. A compound wherein Z=OH, R_1=R_4=R_3=R_6=R_5=R_8=H, R_2=NH_2, R_7=SO_3H is the same meaning as is before defined;

XX. A compound wherein Z=OH, R_1=R_4=R_3=R_6=R_5=R_8=H, R_2=NH_2, R_7=OSO_3H is the same meaning as is before defined;

XXI. A compound wherein Z=OH, R_1=R_3=R_5=R_4=R_7=R_6=H, R_2=NH_2, R_8=SO_3H is the same meaning as is before defined;

XXII. A compound wherein Z=OH, R_1=R_3=R_5=R_4=R_7=R_6=H, R_2=NH_2, R_8=OSO_3H is the same meaning as is before defined;

XXIII. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6= R_7=R_8=H, R_1=$NHSO_3H$ is the same meaning as is before defined;

XXIV. A compound wherein $Z=NH_2$, $R_2=R_3=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_1=CH_2SO_3H$ is the same meaning as is before defined;

XXV. A compound wherein $Z=NH_2$, $R_2=R_3=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_1=CH_2OSO_3H$ is the same meaning as is before defined;

XXVI. A compound wherein $Z=NH_2$, $R_2=R_3=R_4=$ $R_5=R_6=R_7=R_8=H$, $R_1=SO_3H$ is the same meaning as is before defined;

XXVII. A compound wherein $Z=NH_2$, $R_2=R_3=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_1=OSO_3H$ is the same meaning as is before defined;

XXVIII. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_2=NHSO_3H$ is the same meaning as is before defined;

XXIX. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_2=CH_2SO_3H$ is the same meaning as is before defined;

XXX. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=$ $R_5=R_6=R_7=R_8=H$, $R_2=SO_3H$ is the same meaning as is before defined;

XXXI. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_2=OSO_3H$ is the same meaning as is before defined;

XXXII. A compound wherein $Z=NH_2$, $R_1=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_2=NH_2$, $R_3=SO_3H$ is the same meaning as is before defined;

XXXIII. A compound wherein $Z=NH_2$, $R_1=R_4=R_5=R_6=$ $R_7=R_8=H$, $R_2=NH_2$, $R_3=OSO_3H$ is the same meaning as is before defined;

XXXIV. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_6=R_7=R_8=$ H, $R_2=NH_2$, $R_4=SO_3H$ is the same meaning as is before defined;

XXXV. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_6=R_7=R_8=$ H, $R_2=NH_2$, $R_4=OSO_3H$ is the same meaning as is before defined;

XXXVI. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=$ $R_7=R_8=H$, $R_2=NH_2$, $R_5=SO_3H$ is the same meaning as is before defined;

XXXVII. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=$ $R_7=R_8=H$, $R_2=NH_2$, $R_5=OSO_3H$ is the same meaning as is before defined;

XXXVIII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=$ $R_7=R_8=H$, $R_2=NH_2$, $R_6=SO_3H$ is the same meaning as is before defined;

XXXIX. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=$ $R_7=R_8=H$, $R_2=NH_2$, $R_6=OSO_3H$ is the same meaning as is before defined;

XL. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=R_5=R_8=H$, $R_2=NH_2$, $R_7=SO_3H$ is the same meaning as is before defined;

XLI. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=R_5=R_8=H$, $R_2=NH_2$, $R_7=OSO_3H$ is the same meaning as is before defined;

XLII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=R_7=R_6=H$, $R_2=$ NH_2, $R_8=SO_3H$ is the same meaning as is before defined;

XLIII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=R_7=R_6=H$, $R_2=NH_2$, $R_8=OSO_3H$ is the same meaning as is before defined;

Yet another embodiment of a present invention relates to a compound wherein said compound is non-toxic salts selected from the group consisting of:

I. [L- Aspartic acid, N-Sulfonic acid],

II. [2α,3-dicarboxy, propane-1-sulfonic acid],

III. [2α,3-dicarboxy, propane-1-sulfate],

IV. [1α,2-carboxy ethane sulfonic acid],

V. [1α,2-carboxy ethane sulfate],

VI. [D-aspartic acid, N-sulfonic acid],

VII. [2β,3-carboxy,propane-1-sulfonic acid],

VIII. [2β,3-carboxy,propane-1-sulfate],

IX. [1β,2-carboxy ethane-1-sulfonic acid],

X. [1β,2-carboxy ethane-1-sulfate],

XI. [D-aspartic acid, 3α -sulfonic acid],

XII. [D-aspartic acid, 3α-sulfate],

XIII. [D-aspartic acid, 3β-sulfonic acid],

XIV. [D-aspartic acid, 3β-sulfate],

XV. [L-asparagine,N-sulfonic acid],

XVI. [2α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVII. [2α-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1α-carboxy, 2-carboxamido, ethane sulfonic acid],

XIX. [1α-carboxy, 2-carboxamido, ethane sulfate],

XX. [L-asparagine, 3α-sulfonic acid],

XXI. [L-asparagine, 3α-sulfate],

XXII. [L-asparagine, 3β-sulfonic acid],

XXIII. [L-asparagine, 3β-sulfate,

XXIV. [D-asparagine, N-sulfonic acid],

XXV. [2β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXVI. [2β-carboxy, 3-carboxamido, propane-1-sulfate],

XXVII. [1β-carboxy, 2-carboxamido, ethane sulfonic acid],

XXVIII. [1β-carboxy, 2-carboxamido, ethane sulfate],

XXIX. [D-asparagine, 3α-sulfonic acid],

XXX. [D-asparagine, 3α-sulfate],

XXXI. [D-asparagine, 3β-sulfonic acid],

XXXII. [D-asparagine, 3β-sulfate],

XXXIII. [L-glutamic acid, N-sulfonic acid],

XXXIV. [2α,4-dicarboxy, butane-1-sulfonic acid],

XXXV. [2α, 4-dicarboxy, butane-1-sulfate],

XXXVI. [1α, 3-dicarboxy, propane sulfonic acid],

XXXVII. [1α, 3-dicarboxy, propane sulfate],

XXXVIII. [1β, 3-dicarboxy, propane sulfate],

XXXIX. [1β, 3-dicarboxy, propane sulfonic acid],

Yet another embodiment of a present invention relates to a compound wherein said compound is non-toxic salts selected from the group consisting of:

I. [D-glutamic acid, N-sulfonic acid],

II. [2β, 4-dicarboxy, butane-1-sulfonic acid],

III. [2β, 4-dicarboxy, butane-1-sulfate],

IV. [D-glutamic acid, 3α-sulfonic acid],

V. [D-glutamic acid, 3α-sulfate],

VI. [D-glutamic acid, 3β-sulfonic acid],

VII. [D-glutamic acid, 3β-sulfate],

VIII. [D-glutamic acid, 4α-sulfonic acid],

IX. [D-glutamic acid, 4α-sulfate],

X. [D-glutamic acid, 4β-sulfonic acid],

XI. [D-glutamic acid, 3β-sulfate],

XII. [L-glutamine, N-sulfonic acid],

XIII. [2α-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XIV. [2α-carboxy, 4-carboxamido, butane-1-sulfate],

XV. [1α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVI. [1α-carboxy, 3-carboxamido, propane-1-sulfate],

XVII. [1β-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XIX. [D-glutamine, N-sulfonic acid],

XX. [2β-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XXI. [2β-carboxy, 4-carboxamido, butane-1-sulfate],

XXII. [D-glutamine, 3α-sulfonic acid],

XXIII. [D-glutamine, 3α-sulfate],

XXIV. [D-glutamine, 3β-sulfonic acid],

XXV. [D-glutamine, 3β-sulfate],

XXVI. [D-glutamine, 4α-sulfonic acid],

XXVII. [D-glutamine, 4α-sulfate],

XXVIII. [D-glutamine, 4β-sulfonic acid],

XXIX. [D-glutamine, 4β-sulfate],

XXX. [L-homoglutamic acid, N-sulfonic acid],

XXXI. [Pentane-2α, 5-dicarboxy-1-sulfonic acid],

XXXII. [Pentane-2α, 5-dicarboxy-1-sulfate],

XXXIII. [Butane-1α, 4-dicarboxy-1-sulfonic acid],

XXXIV. [Butane-1α, 4-dicarboxy-1-sulfate],

XXXV. [D-homoglutamic acid, N-sulfonic acid],

XXXVI. [Pentane-2β, 5-dicarboxy-1-sulfonic acid],

XXXVII. [Pentane-2β, 5-dicarboxy-1-sulfate],

XXXVIII. [Butane-1β, 4-dicarboxy-1-sulfonic acid],

XXXIX. [Butane-1β, 4-dicarboxy-1-sulfate],

Yet another embodiment of a present invention relates to a compound said compound is non-toxic salts selected from the group consisting of:

I. [D-homoglutamic acid, 3α-sulfonic acid],

II. [D-homoglutamic acid, 3α-sulfate],

III. [D-homoglutamic acid, 3β-sulfonic acid],

IV. [D-homoglutamic acid, 3β-sulfate],

V. [D-homoglutamic acid, 4α-sulfonic acid],

VI. [D-homoglutamic acid, 4α-sulfate],

VII. [D-homoglutamic acid, 4β-sulfonic acid],

VIII. [D-homoglutamic acid, 4β-sulfate],

IX. [D-homoglutamic acid, 5α-sulfate],

X. [D-homoglutamic acid, 5α-sulfate],

XI. [D-homoglutamic acid, 5β-sulfonic acid],

XII. [D-homoglutamic acid, 5β-sulfate],

XIII. [L-homoglutamine, N-sulfonic acid],

XIV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfonic acid],

XV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfate],

XVI. [Butane-1α-carboxy, 4-carboxamido-1-sulfonic acid],

XVII. [Butane-1α-carboxy, 4-carboxamido-1-sulfate],

XVIII. [D-homoglutamine, N-sulfonic acid],

XIX. [Pentane-2β-carboxy, 5-carboxamido-1-sulfonic acid],

XX. [Butane-1 β -carboxy, 4-carboxamido-1-sulfonic acid],

XXI. [Butane-1 β -carboxy, 4-carboxamido-1-sulfate],

XXII. [D-homoglutamine, 3α-sulfonic acid],

XXIII. [D-homoglutamine, 3α-sulfate],

XXIV. [D-homoglutamine, 3β-sulfonic acid],

XXV. [D-homoglutamine, 3β-sulfate],

XXVI. [D-homoglutamine, 4α-sulfonic acid],

XXVII. [D-homoglutamine, 4α-sulfate],

XXVIII. [D-homoglutamine, 4β-sulfonic acid],

XXIX. [D-homoglutamine, 4β-sulfate],

XXX. [D-homoglutamine, 5α-sulfonic acid],

XXXI. [D-homoglutamine, 5α-sulfate],

XXXII. [D-homoglutamine, 5β-sulfonic acid] and

XXXIII. [D-homoglutamine, 5β-sulfate].

Yet another embodiment of a present invention relates to a compound said compound is selected from the group consisting of aspartic acid, asparagine and corresponding de-amino analogs:

I. [L- Aspartic acid, N-Sulfonic acid],

II. [2α,3-dicarboxy, propane-1-sulfonic acid],

III. [2α,3-dicarboxy, propane-1-sulfate],

IV. [1α,2-carboxy ethane sulfonic acid],

V. [1α,2-carboxy ethane sulfate],

VI. [D-aspartic acid, N-sulfonic acid],

VII. [2β,3-carboxy,propane-1-sulfonic acid],

VIII. [2β,3-carboxy,propane-1-sulfate],

IX. [1β,2-carboxy ethane-1-sulfonic acid],

X. [1β,2-carboxy ethane-1-sulfate],

XI. [D-aspartic acid, 3α -sulfonic acid],

XII. [D-aspartic acid, 3α-sulfate],

XIII. [D-aspartic acid, 3β-sulfonic acid],

XIV. [D-aspartic acid, 3β-sulfate],

XV. [L-asparagine,N-sulfonic acid],

XVI. [2α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVII. [2α-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1α-carboxy, 2-carboxamido, ethane sulfonic acid],

XIX. [1α-carboxy, 2-carboxamido, ethane sulfate],

XX. [L-asparagine, 3α-sulfonic acid],

XXI. [L-asparagine, 3α-sulfate],

XXII. [L-asparagine, 3β-sulfonic acid],

XXIII. [L-asparagine, 3β-sulfate,

XXIV. [D-asparagine, N-sulfonic acid],

XXV. [2β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXVI. [2β-carboxy, 3-carboxamido, propane-1-sulfate],

XXVII. [1β-carboxy, 2-carboxamido, ethane sulfonic acid],

XXVIII. [1β-carboxy, 2-carboxamido, ethane sulfate],

XXIX. [D-asparagine, 3α-sulfonic acid],

XXX. [D-asparagine, 3α-sulfate],

XXXI. [D-asparagine, 3β-sulfonic acid],

XXXII. [D-asparagine, 3β-sulfate],

Yet another embodiment of a present invention relates to a compound said compound is selected from the group consisting of glutamic acid, glutamine and corresponding de-amino analogs:

I. [L-glutamic acid, N-sulfonic acid],

II. [2α,4-dicarboxy, butane-1-sulfonic acid],

III. [2α, 4-dicarboxy, butane-1-sulfate],

IV. [1α, 3-dicarboxy, propane sulfonic acid],

V. [1α, 3-dicarboxy, propane sulfate],

VI. [1β, 3-dicarboxy, propane sulfate],

VII. [1β, 3-dicarboxy, propane sulfonic acid],

VIII. [D-glutamic acid, N-sulfonic acid],

IX. [2β, 4-dicarboxy, butane-1-sulfonic acid],

X. [2β, 4-dicarboxy, butane-1-sulfate],

XI. [D-glutamic acid, 3α-sulfonic acid],

XII. [D-glutamic acid, 3α-sulfate],

XIII. [D-glutamic acid, 3β-sulfonic acid],

XIV. [D-glutamic acid, 3β-sulfate],

XV. [D-glutamic acid, 4α-sulfonic acid],

XVI. [D-glutamic acid, 4α-sulfate],

XVII. [D-glutamic acid, 4β-sulfonic acid],

XVIII. [D-glutamic acid, 3β-sulfate],

XIX. [L-glutamine, N-sulfonic acid],

XX. [2α-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XXI. [2α-carboxy, 4-carboxamido, butane-1-sulfate],

XXII. [1α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXIII. [1α-carboxy, 3-carboxamido, propane-1-sulfate],

XXIV. [1β-carboxy, 3-carboxamido, propane-1-sulfate],

XXV. [1β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXVI. [D-glutamine, N-sulfonic acid],

XXVII. [2β-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XXVIII. [2β-carboxy, 4-carboxamido, butane-1-sulfate],

XXIX. [D-glutamine, 3α-sulfonic acid],

XXX. [D-glutamine, 3α-sulfate],

XXXI. [D-glutamine, 3β-sulfonic acid],

XXXII. [D-glutamine, 3β-sulfate],

XXXIII. [D-glutamine, 4α-sulfonic acid],

XXXIV. [D-glutamine, 4α-sulfate],

XXXV. [D-glutamine, 4β-sulfonic acid],

XXXVI. [D-glutamine, 4β-sulfate],

XXXVII. [L-homoglutamic acid, N-sulfonic acid],

XXXVIII. [Pentane-2α, 5-dicarboxy-1-sulfonic acid],

XXXIX. [Pentane-2α, 5-dicarboxy-1-sulfate],

XL. [Butane-1α, 4-dicarboxy-1-sulfonic acid],

XLI. [Butane-1α, 4-dicarboxy-1-sulfate],

Yet another embodiment of a present invention relates to a compound wherein said compound is selected from the group consisting of homoglutamic acid, homoglutamine and corresponding de-amino analogs:

I. [D-homoglutamic acid, N-sulfonic acid],

II. [Pentane-2β, 5-dicarboxy-1-sulfonic acid],

III. [Pentane-2β, 5-dicarboxy-1-sulfate],

IV. [Butane-1β, 4-dicarboxy-1-sulfonic acid],

V. [Butane-1β, 4-dicarboxy-1-sulfate],

VI. [D-homoglutamic acid, 3α-sulfonic acid],

VII. [D-homoglutamic acid, 3α-sulfate],

VIII. [D-homoglutamic acid, 3β-sulfonic acid],

IX. [D-homoglutamic acid, 3β-sulfate],

X. [D-homoglutamic acid, 4α-sulfonic acid],

XI. [D-homoglutamic acid, 4α-sulfate],

XII. [D-homoglutamic acid, 4β-sulfonic acid],

XIII. [D-homoglutamic acid, 4β-sulfate],

XIV. [D-homoglutamic acid, 5α-sulfate],

XV. [D-homoglutamic acid, 5α-sulfate],

XVI. [D-homoglutamic acid, 5β-sulfonic acid],

XVII. [D-homoglutamic acid, 5β-sulfate],

XVIII. [L-homoglutamine, N-sulfonic acid],

XIX. [Pentane-2α-carboxy, 5-carboxamido-1-sulfonic acid],

XX. [Pentane-2α-carboxy, 5-carboxamido-1-sulfate],

XXI. [Butane-1α-carboxy, 4-carboxamido-1-sulfonic acid],

XXII. [Butane-1α-carboxy, 4-carboxamido-1-sulfate],

XXIII. [D-homoglutamine, N-sulfonic acid],

XXIV. [Pentane-2β-carboxy, 5-carboxamido-1-sulfonic acid],

XXV. [Butane-1 β -carboxy, 4-carboxamido-1-sulfonic acid],

XXVI. [Butane-1 β -carboxy, 4-carboxamido-1-sulfate],

XXVII. [D-homoglutamine, 3α-sulfonic acid],

XXVIII. [D-homoglutamine, 3α-sulfate],

XXIX. [D-homoglutamine, 3β-sulfonic acid],

XXX. [D-homoglutamine, 3β-sulfate],

XXXI. [D-homoglutamine, 4α-sulfonic acid],

XXXII. [D-homoglutamine, 4α-sulfate],

XXXIII. [D-homoglutamine, 4β-sulfonic acid],

XXXIV. [D-homoglutamine, 4β-sulfate],

XXXV. [D-homoglutamine, 5α-sulfonic acid],

XXXVI. [D-homoglutamine, 5α-sulfate],

XXXVII. [D-homoglutamine, 5β-sulfonic acid] and

XXXVIII. [D-homoglutamine, 5β-sulfate].

Still another embodiment of the present invention relates to a process for preparing L-glutamyl N-sulfonic acid from glutamic acid mono tertiary butyl ester comprising the steps of:

a) adding L-glutamyl acid mono tertiary butyl ester portion wise to a solution of SO_2Cl_2 in dry CH_2Cl_2 at 0°C) and Et_3N (3 eq.) to obtain a solution,

b) stirring the solution for a time period in the range of 5 to 10 hrs at room temperature unless thin layer chromatography (TLC) shows complete consumption of starting material and evaporating the solvent present in TLC and crude is drying in vaccum,

c) adding water to dried crude and stirring the slurry for a time period in the range of 0.5 to 3 hr,

d) adding 45 ml CH_2Cl_2 and 3 equivalent of TFA at 0°Cto the solution and stirring for 24 hrs

e) evaporating the solvent and drying in vacuum to obtain the product L-glutamyl , N-sulfonic acid.

A further embodiment of the present invention relates to for preparing L- glutamyl, N-sulfonic acid from glutamyl acid di tertiary butyl ester comprising the steps of:

a. adding L-aspartic acid di tertiary butyl ester portion wise to a solution of SO_2Cl_2 in dry CH_2Cl_2 at 0°C) and Et_3N (3 eq.) to obtain a solution,

b. stirring the solution for a time period in the range of 5 to 10 hrs at room temperature unless thin layer chromatography shows complete consumption

of starting material evaporating the solvent present in TLC and crude is drying in vaccum,

c. adding water to dried crude and stirring the slurry for a time period in the range of 0.5 to 3 hr,

d. adding 45 ml CH_2Cl_2 and 3 equivalent of TFA at 0°Cto the solution and stirring for 24 hrs

e. evaporating the solvent and drying in vacuum to obtain the product L-aspartyl, N-sulfonic acid.

A further embodiment of the present invention relates to a process for preparing L-Aspartyl, N-sulfonic acid from L-aspartic acid di tertiary butyl ester comprising the steps of:

a. adding L-aspartic acid di tertiary butyl ester portion wise to a solution of SO_2Cl_2 in dry CH_2Cl_2 at 0°C) and Et_3N (3 eq.) to obtain a solution,

b. stirring the solution for a time period in the range of 5 to 10 hrs at room temperature unless thin layer chromatography shows complete consumption of starting material evaporating the solvent and drying the crude in vacuum,

c. adding water to dried crude and stirring the slurry for a time period in the range of 0.5 to 3 hr,

d. adding 45 ml CH_2Cl_2 and 3 equivalent of TFA at 0°Cto the solution and stirring for 24 hrs

e. evaporating the solvent and drying in vacuum to obtain the product L-aspartyl, N-sulfonic acid.

A Further another embodiment of the present invention relates to process for preparing L-Homoglutamyl, N-sulfonic acid from L-Homoglutamic acid di tertiary butyl ester comprising the steps of:

a. adding L-Homoglutamic acid di tertiary butyl ester portion-wise to a solution of SO_2Cl_2 in dry CH_2Cl_2 at 0°C and Et_3N,

b. stirring the solution for 8 hrs at r. t. till TLC showed complete consumption of starting material evaporating the solvent and drying the crude in vacuum,

c. adding water to it to obtain a slurry which is stirred for 1 hr,

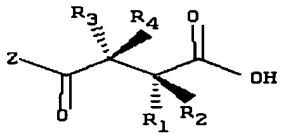
d. adding to the slurry 45 ml CH_2Cl_2 followed by 3 eq of TFA at 0°C and stirring the resulting solution for 24 hrs,

e. evaporating and drying the solution in vacuum to obtain the product L-homoglutamyl, N-sulfonic acid.

A further embodiment of the present invention relates to a Pharmaceutical composition comprising the effective amount of a compound selected from the general formula Z-OC (C $R_{n1}R_{n2}$) -CO-Z wherein Z = OH or NH_2 and n1 = n2 =1 to 8 along with an additive, excipient , diluents or carrier.

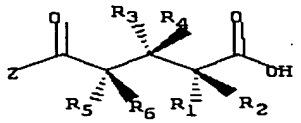
Yet another embodiment of the present invention relates to said composition useful in vaccine formulation to prevent more efficient and faster presentation of antigens to T-cells thereby initiate primary protective Th1 immune response and help in the clearance of the pathogen.

Yet another embodiment of the present invention relates to said composition having a structure as herein and bearing general formula ZOC-CR_3R_4-CR_1R_2-COOH wherein: Z=OH or NH_2, R_1, to R_4 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$



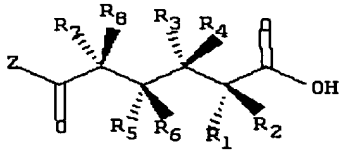
Structure 1

Yet another embodiment of the present invention relates, wherein said compound having a structure as herein and bearing general formula ZOC- CR_5R_6-CR_3R_4-CR_1R_2-COOH wherein: Z=OH or NH_2, R_1 to R_6 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$



Structure 2

Yet another embodiment of the present invention relates said compound having structure as herein and bearing general formula ZOC-CR_7R_8-CR_5R_6-CR_3R_4-CR_1R_2-COOH wherein: Z=OH or NH_2, R_1 to R_8 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$



structure 3

Yet another embodiment of the present invention relates to said compound in non-toxic to monocytes.

Yet another embodiment of the present invention relates said compound in non-toxic to macrophages.

Yet another embodiment of the present invention relates additives are different divalent metal cations such as Mg, Ca and Zn.

Yet another embodiment of the present invention wherein, additives are amino acid/ dicarboxylic acid derivatives and their pharmaceutically acceptable selected alkali/ alkaline earth metal salts.

Yet another embodiment of the present invention, wherein the compound is selected from the group consisting of:

I. [L- Aspartic acid, N-Sulfonic acid],
II. [2α,3-dicarboxy, propane-1-sulfonic acid],
III. [2α,3-dicarboxy, propane-1-sulfate],
IV. [1α,2-carboxy ethane sulfonic acid],

V. [1α,2-carboxy ethane sulfate],

VI. [D-aspartic acid, N-sulfonic acid],

VII. [2β,3-carboxy,propane-1-sulfonic acid],

VIII. [2β,3-carboxy,propane-1-sulfate],

IX. [1β,2-carboxy ethane-1-sulfonic acid],

X. [1β,2-carboxy ethane-1-sulfate],

XI. [D-aspartic acid, 3α -sulfonic acid],

XII. [D-aspartic acid, 3α-sulfate],

XIII. [D-aspartic acid, 3β-sulfonic acid],

XIV. [D-aspartic acid, 3β-sulfate],

XV. [L-asparagine,N-sulfonic acid],

XVI. [2α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVII. [2α-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1α-carboxy, 2-carboxamido, ethane sulfonic acid],

XIX. [1α-carboxy, 2-carboxamido, ethane sulfate],

XX. [L-asparagine, 3α-sulfonic acid],

XXI. [L-asparagine, 3α-sulfate],

XXII. [L-asparagine, 3β-sulfonic acid],

XXIII. [L-asparagine, 3β-sulfate,

XXIV. [D-asparagine, N-sulfonic acid],

XXV. [2β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXVI. [2β-carboxy, 3-carboxamido, propane-1-sulfate],

XXVII. [1β-carboxy, 2-carboxamido, ethane sulfonic acid],

XXVIII. [1β-carboxy, 2-carboxamido, ethane sulfate],

XXIX. [D-asparagine, 3α-sulfonic acid],

XXX. [D-asparagine, 3α-sulfate],

XXXI. [D-asparagine, 3β-sulfonic acid],

XXXII. [D-asparagine, 3β-sulfate],

XXXIII. [L-glutamic acid, N-sulfonic acid],

XXXIV. [2α,4-dicarboxy, butane-1-sulfonic acid],

XXXV. [2α, 4-dicarboxy, butane-1-sulfate],

XXXVI. [1α, 3-dicarboxy, propane sulfonic acid],

XXXVII. [1α, 3-dicarboxy, propane sulfate],

XXXVIII. [1β, 3-dicarboxy, propane sulfate],

XXXIX. [1β, 3-dicarboxy, propane sulfonic acid],

Yet another embodiment of the present invention, wherein the compound is selected from the group consisting of:

I. [D-glutamic acid, N-sulfonic acid],

II. 2β, 4-dicarboxy, butane-1-sulfonic acid],

III. [2β, 4-dicarboxy, butane-1-sulfate],

IV. [D-glutamic acid, 3α-sulfonic acid],

V. [D-glutamic acid, 3α-sulfate],

VI. [D-glutamic acid, 3β-sulfonic acid],

VII. [D-glutamic acid, 3β-sulfate],

VIII. [D-glutamic acid, 4α-sulfonic acid],

IX. [D-glutamic acid, 4α-sulfate],

X. [D-glutamic acid, 4β-sulfonic acid],

XI. [D-glutamic acid, 3β-sulfate],

XII. [L-glutamine, N-sulfonic acid],

XIII. [2α-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XIV. [2α-carboxy, 4-carboxamido, butane-1-sulfate],

XV. [1α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVI. [1α-carboxy, 3-carboxamido, propane-1-sulfate],

XVII. [1β-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XIX. [D-glutamine, N-sulfonic acid],

XX. [2β-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XXI. [2β-carboxy, 4-carboxamido, butane-1-sulfate],

XXII. [D-glutamine, 3α-sulfonic acid],

XXIII. [D-glutamine, 3α-sulfate],

XXIV. [D-glutamine, 3β-sulfonic acid],

XXV. [D-glutamine, 3β-sulfate],

XXVI. [D-glutamine, 4α-sulfonic acid],

XXVII. [D-glutamine, 4α-sulfate],

XXVIII. [D-glutamine, 4β-sulfonic acid],

XXIX. [D-glutamine, 4β-sulfate],

XXX. [L-homoglutamic acid, N-sulfonic acid],

XXXI. [Pentane-2α, 5-dicarboxy-1-sulfonic acid],

XXXII. [Pentane-2α, 5-dicarboxy-1-sulfate],

XXXIII. [Butane-1α, 4-dicarboxy-1-sulfonic acid],

XXXIV. [Butane-1α, 4-dicarboxy-1-sulfate],

XXXV. [D-homoglutamic acid, N-sulfonic acid],

XXXVI. [Pentane-2β, 5-dicarboxy-1-sulfonic acid],

XXXVII. [Pentane-2β, 5-dicarboxy-1-sulfate],

XXXVIII. [Butane-1β, 4-dicarboxy-1-sulfonic acid],

XXXIX. [Butane-1β, 4-dicarboxy-1-sulfate],

Yet another embodiment of the present invention, wherein the compound is selected from the group consisting of

I. [D-homoglutamic acid, 3α-sulfonic acid],

II. [D-homoglutamic acid, 3α-sulfate],

III. [D-homoglutamic acid, 3β-sulfonic acid],

IV. [D-homoglutamic acid, 3β-sulfate],

V. [D-homoglutamic acid, 4α-sulfonic acid],

VI. [D-homoglutamic acid, 4α-sulfate],

VII. [D-homoglutamic acid, 4β-sulfonic acid],

VIII. [D-homoglutamic acid, 4β-sulfate],

IX. [D-homoglutamic acid, 5α-sulfate],

X. [D-homoglutamic acid, 5α-sulfate],

XI. [D-homoglutamic acid, 5β-sulfonic acid],

XII. [D-homoglutamic acid, 5β-sulfate],

XIII. [L-homoglutamine, N-sulfonic acid],

XIV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfonic acid],

XV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfate],

XVI. [Butane-1α-carboxy, 4-carboxamido-1-sulfonic acid],

XVII. [Butane-1α-carboxy, 4-carboxamido-1-sulfate],

XVIII. [D-homoglutamine, N-sulfonic acid],

XIX. [Pentane-2β-carboxy, 5-carboxamido-1-sulfonic acid],

XX. [Butane-1 β -carboxy, 4-carboxamido-1-sulfonic acid],

XXI. [Butane-1 β -carboxy, 4-carboxamido-1-sulfate],

XXII. [D-homoglutamine, 3α-sulfonic acid],

XXIII. [D-homoglutamine, 3α-sulfate],

XXIV. [D-homoglutamine, 3β-sulfonic acid],

XXV. [D-homoglutamine, 3β-sulfate],

XXVI. [D-homoglutamine, 4α-sulfonic acid],

XXVII. [D-homoglutamine, 4α-sulfate],

XXVIII. [D-homoglutamine, 4β-sulfonic acid],

XXIX. [D-homoglutamine, 4β-sulfate],

XXX. [D-homoglutamine, 5α-sulfonic acid],

XXXI. [D-homoglutamine, 5α-sulfate],

XXXII. [D-homoglutamine, 5β-sulfonic acid] and

XXXIII. [D-homoglutamine, 5β-sulfate].

Yet another embodiment of the present invention, wherein novel sulfonic acid / sulfate derivatives of the formulae ZOC-CR_3R_4-CR_1R_2-COOH wherein: Z=OH or NH_2, R_1, to R_4 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$

I. A compound wherein Z=OH, R_2=R_3=R_4=H, R_1= $NHSO_3H$ is the same meaning as is before defined;

II. A compound wherein Z=OH, R_2=R_3=R_4=H, R_1= CH_2SO_3H is the same meaning as is before defined;

III. A compound wherein Z=OH, R_2=R_3=R_4=H, R_1= CH_2OSO_3H is the same meaning as is before defined;

IV. A compound wherein Z=OH, R_2=R_3=R_4=H, R_1=SO_3H is the same meaning as is before defined;

V. A compound wherein Z=OH, R_2=R_3=R_4=H, R_1=OSO_3H is the same meaning as is before defined;

VI. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2= $NHSO_3H$ is the same meaning as is before defined;

VII. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2= CH_2SO_3H is the same meaning as is before defined;

VIII. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2= CH_2OSO_3H is the same meaning as is before defined;

IX. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2=SO_3H is the same meaning as is before defined;

X. A compound wherein Z=OH, R_1=R_3=R_4=H, R_2=OSO_3H is the same meaning as is before defined;

XI. A compound wherein Z=OH, R_1=R_4=H, R_2=NH_2, R_3=SO_3H is the same meaning as is before defined;

XII. A compound wherein Z=OH, R_1=R_4=H, R_2=NH_2, R_3=SO_3H is the same meaning as is before defined;

XIII. A compound wherein Z=OH, R_1=R_3=H, R_2=NH_2, R_4=SO_3H is the same meaning as is before defined;

XIV. A compound wherein Z=OH, R_1=R_3=H, R_2=NH_2, R_4=OSO_3H is the same meaning as is before defined;

XV. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1=$NHSO_3H$ is the same meaning as is before defined;

XVI. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1=CH_2SO_3H is the same meaning as is before defined;

XVII. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1= CH_2OSO_3H is the same meaning as is before defined;

XVIII. A compound wherein Z=NH_2, R_2=R_3=R_4=H, R_1=SO_3H is the same meaning as is before defined;

XIX. A compound wherein $Z=NH_2$, $R_2=R_3=R_4=H$, $R_1=OSO_3H$ is the same meaning as is before defined;

XX. A compound wherein $Z=NH_2$, $R_1=R_4=H$, $R_2=NH_2$, $R_3= SO_3H$ is the same meaning as is before defined;

XXI. A compound wherein $Z=NH_2$, $R_1=R_4=H$, $R_2=NH_2$, $R_3= OSO_3H$ is the same meaning as is before defined;

XXII. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2=NH_2$, $R_4= SO_3H$ is the same meaning as is before defined;

XXIII. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2= NH_2$, $R_4= OSO_3H$ is the same meaning as is before defined;

XXIV. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2= NHSO_3H$ is the same meaning as is before defined;

XXV. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2= CH_2SO_3H$ is the same meaning as is before defined;

XXVI. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2= CH_2OSO_3H$ is the same meaning as is before defined;

XXVII. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2=SO_3H$ is the same meaning as is before defined;

XXVIII. A compound wherein $Z=NH_2$, $R_1=R_3=R_4=H$, $R_2=OSO_3H$ is the same meaning as is before defined;

XXIX. A compound wherein $Z=NH_2$, $R_1=R_4=H$, $R_2=NH_2$, $R_3= SO_3H$ is the same meaning as is before defined;

XXX. A compound wherein $Z=NH_2$, $R_1=R_4=H$, $R_2=NH_2$, $R_3= OSO_3H$ is the same meaning as is before defined;

XXXI. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2=NH_2$, $R_4=SO_3H$ is the same meaning as is before defined;

XXXII. A compound wherein $Z=NH_2$, $R_1=R_3=H$, $R_2=NH_2$, $R_4=OSO_3H$ is the same meaning as is before defined.

Yet another embodiment of the present invention, wherein novel sulfonic acid / sulfate derivatives of the formulae $ZOC\text{-}CR_5R_6\text{-}CR_3R_4\text{-}CR_1R_2\text{-}COOH$, wherein:

Z=OH or NH_2, R_1, to R_6 denotes H, NH_2, SO_3H, or OSO_3H, CH_2-SO_3H, CH_2-OSO_3H, $NHSO_3H$

I. A compound wherein Z=OH, R_2=R_3=R_4=R_5=R_6=H, R_1=$NHSO_3H$ is the same meaning as is before defined;

II. A compound wherein Z=OH, R_2=R_3=R_4=R_5=R_6=H, R_1= CH_2SO_3H is the same meaning as is before defined;

III. A compound wherein Z=OH, R_2=R_3=R_4=R_5=R_6=H, R_1=CH_2OSO_3H is the same meaning as is before defined;

IV. A compound wherein Z=OH, R_2=R_3=R_4= R_5=R_6=H, R_1= SO_3H is the same meaning as is before defined;

V. A compound wherein Z=OH, R_2=R_3=R_4=R_5=R_6=H, R_1=OSO_3H is the same meaning as is before defined;

VI. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6=H, R_2=OSO_3H is the same meaning as is before defined;

VII. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6=H, R_2= SO_3H is the same meaning as is before defined;

VIII. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6=H, R_2= $NHSO_3H$ is the same meaning as is before defined;

IX. A compound wherein Z=OH, R_1=R_3=R_4= R_5=R_6=H, R_2= CH_2SO_3H is the same meaning as is before defined;

X. A compound wherein Z=OH, R_1=R_3=R_4= R_5=R_6=H, R_2= CH_2OSO_3H is the same meaning as is before defined;

XI. A compound wherein Z=OH, R_1=R_4=R_5=R_6=H, R_2= NH_2, R_3=SO_3H is the same meaning as is before defined;

XII. A compound wherein Z=OH, R_1=R_4=R_5=R_6=H, R_2= NH_2, R_3=OSO_3H is the same meaning as is before defined;

XIII. A compound wherein Z=OH, R_1=R_3=R_5=R_6=H, R_2= NH_2, R_4= SO_3H is the same meaning as is before defined;

XIV. A compound wherein Z=OH, R_1=R_3=R_5=R_6=H, R_2= NH_2, R_4=OSO_3H is the same meaning as is before defined;

XV. A compound wherein Z=OH, R_1=R_4= R_3=R_6=H, R_2= NH_2, R_5=SO_3H is the same meaning as is before defined;

XVI. A compound wherein Z=OH, R_1=R_4=R_3=R_6=H, R_2= NH_2, R_5=OSO_3H is the same meaning as is before defined;

XVII. A compound wherein Z=OH, R_1=R_3=R_5=R_4=H, R_2= NH_2, R_6=SO_3H is the same meaning as is before defined;

XVIII. A compound wherein Z=OH, R_1=R_3=R_5=R_4=H, R_2= NH_2, R_6=OSO_3H is the same meaning as is before defined;

XIX. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1=$NHSO_3H$ is the same meaning as is before defined;

XX. A compound wherein Z=NH_2, R_2=R_3=R_4= R_5=R_6=H, R_1=CH_2SO_3H is the same meaning as is before defined;

XXI. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1= CH_2OSO_3H is the same meaning as is before defined;

XXII. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1=SO_3H is the same meaning as is before defined;

XXIII. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6=H, R_1= OSO_3H is the same meaning as is before defined;

XXIV. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= OSO_3H is the same meaning as is before defined;

XXV. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= SO_3H is the same meaning as is before defined;

XXVI. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= $NHSO_3H$ is the same meaning as is before defined;

XXVII. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2=CH_2SO_3H is the same meaning as is before defined;

XXVIII. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6=H, R_2= CH_2OSO_3H is the same meaning as is before defined;

XXIX. A compound wherein Z=NH_2, R_1=R_4=R_5=R_6=H, R_2= NH_2, R_3=SO_3H is the same meaning as is before defined;

XXX. A compound wherein $Z=NH_2$, $R_1=R_4=R_5=R_6=H$, $R_2= NH_2$, $R_3=OSO_3H$ is the same meaning as is before defined;

XXXI. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_6=H$, $R_2= NH_2$, $R_4=SO_3H$ is the same meaning as is before defined;

XXXII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_6=H$, $R_2= NH_2$, $R_4=OSO_3H$ is the same meaning as is before defined;

XXXIII. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=H$, $R_2= NH_2$, $R_5=SO_3H$ is the same meaning as is before defined;

XXXIV. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=H$, $R_2= NH_2$, $R_5=OSO_3H$ is the same meaning as is before defined;

XXXV. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=H$, $R_2= NH_2$, $R_6=SO_3H$ is the same meaning as is before defined;

XXXVI. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=H$, $R_2= NH_2$, $R_6=OSO_3H$ is the same meaning as is before defined.

Yet another embodiment of the present invention, wherein novel sulfonic acid / sulfate derivatives of the formulae $ZOC\text{-}CR_7R_8\text{-}CR_5R_6\text{-}CR_3R_4\text{-}CR_1R_2\text{-}COOH$, wherein:Z=OH or NH_2, R_1, to R_8 denotes H, NH_2, SO_3H, or OSO_3H, $CH_2\text{-}SO_3H$, $CH_2\text{-}OSO_3H$, $NHSO_3H$

I. A compound wherein $Z=OH$, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1=NHSO_3H$ is the same meaning as is before defined;

II. A compound wherein $Z=OH$, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1= -CH_2SO_3H$ is the same meaning as is before defined;

III. A compound wherein $Z=OH$, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1=CH_2OSO_3H$ is the same meaning as is before defined;

IV. A compound wherein $Z=OH$, $R_2=R_3=R_4= R_5=R_6=R_7=R_8=H$, $R_1=SO_3H$ is the same meaning as is before defined;

V. A compound wherein $Z=OH$, $R_2=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_1=OSO_3H$ is the same meaning as is before defined;

VI. A compound wherein $Z=OH$, $R_1=R_3=R_4=R_5=R_6= R_7=R_8=H$, $R_2=NHSO_3H$ is the same meaning as is before defined;

VII. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6= R_7=R_8=H, R_2=CH_2SO_3H is the same meaning as is before defined;

VIII. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6= R_7=R_8=H, R_2=CH_2OSO_3H is the same meaning as is before defined;

IX. A compound wherein Z=OH, R_1=R_3=R_4= R_5=R_6=R_7=R_8=H, R_2=SO_3H is the same meaning as is before defined;

X. A compound wherein Z=OH, R_1=R_3=R_4=R_5=R_6= R_7=R_8=H, R_2=OSO_3H is the same meaning as is before defined;

XI. A compound wherein Z=OH, R_1=R_4= R_5=R_6= R_7=R_8=H, R_2=NH_2, R_3=SO_3H is the same meaning as is before defined;

XII. A compound wherein Z=OH, R_1=R_4=R_5=R_6=R_7=R_8=H, R_2=NH_2, R_3=OSO_3H is the same meaning as is before defined;

XIII. A compound wherein Z=OH, R_1=R_3=R_5=R_6= R_7=R_8=H, R_2= NH_2, R_4=SO_3H is the same meaning as is before defined;

XIV. A compound wherein Z=OH, R_1=R_3=R_5=R_6=R_7=R_8=H, R_2=NH_2, R_4=OSO_3H is the same meaning as is before defined;

XV. A compound wherein Z=OH, R_1=R_4= R_3=R_6= R_7=R_8=H, R_2=NH_2, R_5=SO_3H is the same meaning as is before defined;

XVI. A compound wherein Z=OH, R_1=R_4=R_3=R_6= R_7=R_8=H, R_2=NH_2, R_5=OSO_3H is the same meaning as is before defined;

XVII. A compound wherein Z=OH, R_1=R_3=R_5=R_4= R_7=R_8=H, R_2=NH_2, R_6=SO_3H is the same meaning as is before defined;

XVIII. A compound wherein Z=OH, R_1=R_3=R_5=R_4= R_7=R_8=H, R_2=NH_2, R_6=OSO_3H is the same meaning as is before defined;

XIX. A compound wherein Z=OH, R_1=R_4=R_3=R_6=R_5=R_8=H, R_2=NH_2, R_7=SO_3H is the same meaning as is before defined;

XX. A compound wherein Z=OH, R_1=R_4=R_3=R_6=R_5=R_8=H, R_2=NH_2, R_7=OSO_3H is the same meaning as is before defined;

XXI. A compound wherein Z=OH, R_1=R_3=R_5=R_4=R_7=R_6=H, R_2=NH_2, R_8=SO_3H is the same meaning as is before defined;

XXII. A compound wherein Z=OH, R_1=R_3=R_5=R_4=R_7=R_6=H, R_2=NH_2, R_8=OSO_3H is the same meaning as is before defined;

XXIII. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6= R_7=R_8=H, R_1=$NHSO_3H$ is the same meaning as is before defined;

XXIV. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6= R_7=R_8=H, R_1=CH_2SO_3H is the same meaning as is before defined;

XXV. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6= R_7=R_8=H, R_1=CH_2OSO_3H is the same meaning as is before defined;

XXVI. A compound wherein Z=NH_2, R_2=R_3=R_4= R_5=R_6=R_7=R_8=H, R_1=SO_3H is the same meaning as is before defined;

XXVII. A compound wherein Z=NH_2, R_2=R_3=R_4=R_5=R_6= R_7=R_8=H, R_1=OSO_3H is the same meaning as is before defined;

XXVIII. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6= R_7=R_8=H, R_2=$NHSO_3H$ is the same meaning as is before defined;

XXIX. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6= R_7=R_8=H, R_2=CH_2SO_3H is the same meaning as is before defined;

XXX. A compound wherein Z=NH_2, R_1=R_3=R_4= R_5=R_6=R_7=R_8=H, R_2=SO_3H is the same meaning as is before defined;

XXXI. A compound wherein Z=NH_2, R_1=R_3=R_4=R_5=R_6= R_7=R_8=H, R_2=OSO_3H is the same meaning as is before defined;

XXXII. A compound wherein Z=NH_2, R_1=R_4=R_5=R_6= R_7=R_8=H, R_2=NH_2, R_3=SO_3H is the same meaning as is before defined;

XXXIII. A compound wherein Z=NH_2, R_1=R_4=R_5=R_6= R_7=R_8=H, R_2=NH_2, R_3=OSO_3H is the same meaning as is before defined;

XXXIV. A compound wherein Z=NH_2, R_1=R_3=R_5=R_6=R_7=R_8= H, R_2=NH_2, R_4=SO_3H is the same meaning as is before defined;

XXXV. A compound wherein Z=NH_2, R_1=R_3=R_5=R_6=R_7=R_8= H, R_2=NH_2, R_4=OSO_3H is the same meaning as is before defined;

XXXVI. A compound wherein Z=NH_2, R_1=R_4=R_3=R_6= R_7=R_8=H, R_2=NH_2, R_5=SO_3H is the same meaning as is before defined;

XXXVII. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=$ $R_7=R_8=H$, $R_2=NH_2$, $R_5=OSO_3H$ is the same meaning as is before defined;

XXXVIII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=$ $R_7=R_8=H$, $R_2=NH_2$, $R_6=SO_3H$ is the same meaning as is before defined;

XXXIX. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=$ $R_7=R_8=H$, $R_2=NH_2$, $R_6=OSO_3H$ is the same meaning as is before defined;

XL. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=R_5=R_8=H$, $R_2=NH_2$, $R_7=SO_3H$ is the same meaning as is before defined;

XLI. A compound wherein $Z=NH_2$, $R_1=R_4=R_3=R_6=R_5=R_8=H$, $R_2=NH_2$, $R_7=OSO_3H$ is the same meaning as is before defined;

XLII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=R_7=R_6=H$, $R_2=$ NH_2, $R_8=SO_3H$ is the same meaning as is before defined;

XLIII. A compound wherein $Z=NH_2$, $R_1=R_3=R_5=R_4=R_7=R_6=H$, $R_2=NH_2$, $R_8=OSO_3H$ is the same meaning as is before defined;

Yet another embodiment of the present invention, wherein said compound is non-toxic salts selected from the group consisting of:

I. [L- Aspartic acid, N-Sulfonic acid],

II. [2α,3-dicarboxy, propane-1-sulfonic acid],

III. [2α,3-dicarboxy, propane-1-sulfate],

IV. [1α,2-carboxy ethane sulfonic acid],

V. [1α,2-carboxy ethane sulfate],

VI. [D-aspartic acid, N-sulfonic acid],

VII. [2β,3-carboxy,propane-1-sulfonic acid],

VIII. [2β,3-carboxy,propane-1-sulfate],

IX. [1β,2-carboxy ethane-1-sulfonic acid],

X. [1β,2-carboxy ethane-1-sulfate],

XI. [D-aspartic acid, 3α -sulfonic acid],

XII. [D-aspartic acid, 3α-sulfate],

XIII. [D-aspartic acid, 3β-sulfonic acid],

XIV. [D-aspartic acid, 3β-sulfate],

XV. [L-asparagine,N-sulfonic acid],

XVI. [2α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVII. [2α-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1α-carboxy, 2-carboxamido, ethane sulfonic acid],

XIX. [1α-carboxy, 2-carboxamido, ethane sulfate],

XX. [L-asparagine, 3α-sulfonic acid],

XXI. [L-asparagine, 3α-sulfate],

XXII. [L-asparagine, 3β-sulfonic acid],

XXIII. [L-asparagine, 3β-sulfate,

XXIV. [D-asparagine, N-sulfonic acid],

XXV. [2β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXVI. [2β-carboxy, 3-carboxamido, propane-1-sulfate],

XXVII. [1β-carboxy, 2-carboxamido, ethane sulfonic acid],

XXVIII. [1β-carboxy, 2-carboxamido, ethane sulfate],

XXIX. [D-asparagine, 3α-sulfonic acid],

XXX. [D-asparagine, 3α-sulfate],

XXXI. [D-asparagine, 3β-sulfonic acid],

XXXII. [D-asparagine, 3β-sulfate],

XXXIII. [L-glutamic acid, N-sulfonic acid],

XXXIV. [2α,4-dicarboxy, butane-1-sulfonic acid],

XXXV. [2α, 4-dicarboxy, butane-1-sulfate],

XXXVI. [1α, 3-dicarboxy, propane sulfonic acid],

XXXVII. [1α, 3-dicarboxy, propane sulfate],

XXXVIII. [1β, 3-dicarboxy, propane sulfate],

XXXIX. [1β, 3-dicarboxy, propane sulfonic acid],

Yet another embodiment of the present invention relates to a composition, wherein said compound is non-toxic salts selected from the group consisting of:

I. [D-glutamic acid, N-sulfonic acid],

II. [2β, 4-dicarboxy, butane-1-sulfonic acid],

III. [2β, 4-dicarboxy, butane-1-sulfate],

IV. [D-glutamic acid, 3α-sulfonic acid],

V. [D-glutamic acid, 3α-sulfate],

VI. [D-glutamic acid, 3β-sulfonic acid],

VII. [D-glutamic acid, 3β-sulfate],

VIII. [D-glutamic acid, 4α-sulfonic acid],

IX. [D-glutamic acid, 4α-sulfate],

X. [D-glutamic acid, 4β-sulfonic acid],

XI. [D-glutamic acid, 3β-sulfate],

XII. [L-glutamine, N-sulfonic acid],

XIII. [2α-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XIV. [2α-carboxy, 4-carboxamido, butane-1-sulfate],

XV. [1α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVI. [1α-carboxy, 3-carboxamido, propane-1-sulfate],

XVII. [1β-carboxy, 3-carboxamido, propane-1-sulfate],

XVIII. [1β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XIX. [D-glutamine, N-sulfonic acid],

XX. [2β-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XXI. [2β-carboxy, 4-carboxamido, butane-1-sulfate],

XXII. [D-glutamine, 3α-sulfonic acid],

XXIII. [D-glutamine, 3α-sulfate],

XXIV. [D-glutamine, 3β-sulfonic acid],

XXV. [D-glutamine, 3β-sulfate],

XXVI. [D-glutamine, 4α-sulfonic acid],

XXVII. [D-glutamine, 4α-sulfate],

XXVIII. [D-glutamine, 4β-sulfonic acid],

XXIX. [D-glutamine, 4β-sulfate],

XXX. [L-homoglutamic acid, N-sulfonic acid],

XXXI. [Pentane-2α, 5-dicarboxy-1-sulfonic acid],

XXXII. [Pentane-2α, 5-dicarboxy-1-sulfate],

XXXIII. [Butane-1α, 4-dicarboxy-1-sulfonic acid],

XXXIV. [Butane-1α, 4-dicarboxy-1-sulfate],

XXXV. [D-homoglutamic acid, N-sulfonic acid],

XXXVI. [Pentane-2β, 5-dicarboxy-1-sulfonic acid],

XXXVII. [Pentane-2β, 5-dicarboxy-1-sulfate],

XXXVIII. [Butane-1β, 4-dicarboxy-1-sulfonic acid],

XXXIX. [Butane-1β, 4-dicarboxy-1-sulfate],

Yet another embodiment of the present invention, wherein said compound is non-toxic salts selected from the group consisting of:

I. [D-homoglutamic acid, 3α-sulfonic acid],

II. [D-homoglutamic acid, 3α-sulfate],

III. [D-homoglutamic acid, 3β-sulfonic acid],

IV. [D-homoglutamic acid, 3β-sulfate],

V. [D-homoglutamic acid, 4α-sulfonic acid],

VI. [D-homoglutamic acid, 4α-sulfate],

VII. [D-homoglutamic acid, 4β-sulfonic acid],

VIII. [D-homoglutamic acid, 4β-sulfate],

IX. [D-homoglutamic acid, 5α-sulfate],

X. [D-homoglutamic acid, 5α-sulfate],

XI. [D-homoglutamic acid, 5β-sulfonic acid],

XII. [D-homoglutamic acid, 5β-sulfate],

XIII. [L-homoglutamine, N-sulfonic acid],

XIV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfonic acid],

XV. [Pentane-2α-carboxy, 5-carboxamido-1-sulfate],

XVI. [Butane-1α-carboxy, 4-carboxamido-1-sulfonic acid],

XVII. [Butane-1α-carboxy, 4-carboxamido-1-sulfate],

XVIII. [D-homoglutamine, N-sulfonic acid],

XIX. [Pentane-2β-carboxy, 5-carboxamido-1-sulfonic acid],

XX. [Butane-1 β -carboxy, 4-carboxamido-1-sulfonic acid],

XXI. [Butane-1 β -carboxy, 4-carboxamido-1-sulfate],

XXII. [D-homoglutamine, 3α-sulfonic acid],

XXIII. [D-homoglutamine, 3α-sulfate],

XXIV. [D-homoglutamine, 3β-sulfonic acid],

XXV. [D-homoglutamine, 3β-sulfate],

XXVI. [D-homoglutamine, 4α-sulfonic acid],

XXVII. [D-homoglutamine, 4α-sulfate],

XXVIII. [D-homoglutamine, 4β-sulfonic acid],

XXIX. [D-homoglutamine, 4β-sulfate],

XXX. [D-homoglutamine, 5α-sulfonic acid],

XXXI. [D-homoglutamine, 5α-sulfate],

XXXII. [D-homoglutamine, 5β-sulfonic acid] and

XXXIII. [D-homoglutamine, 5β-sulfate].

Yet another embodiment of the present invention, wherein said compound is selected from the group consisting of aspartic acid, asparagine and corresponding de-amino analogs:

I. [L- Aspartic acid, N-Sulfonic acid],

II. [2α,3-dicarboxy, propane-1-sulfonic acid],

III. [2α,3-dicarboxy, propane-1-sulfate],

IV. [1α,2-carboxy ethane sulfonic acid],

V. [1α,2-carboxy ethane sulfate],

VI. [D-aspartic acid, N-sulfonic acid],

VII. [2β,3-carboxy,propane-1-sulfonic acid],

VIII. [2β,3-carboxy,propane-1-sulfate],

IX. [1β,2-carboxy ethane-1-sulfonic acid],

X. [1β,2-carboxy ethane-1-sulfate],

XI. [D-aspartic acid, 3α -sulfonic acid],

XII. [D-aspartic acid, 3α-sulfate],

XIII. [D-aspartic acid, 3β-sulfonic acid],

XIV. [D-aspartic acid, 3β-sulfate],

XV. [L-asparagine,N-sulfonic acid],

XVI. [2α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XVII. [2α-carboxy, 3-carboxamido, propane-1-sulfate],
XVIII. [1α-carboxy, 2-carboxamido, ethane sulfonic acid],
XIX. [1α-carboxy, 2-carboxamido, ethane sulfate],
XX. [L-asparagine, 3α-sulfonic acid],
XXI. [L-asparagine, 3α-sulfate],
XXII. [L-asparagine, 3β-sulfonic acid],
XXIII. [L-asparagine, 3β-sulfate,
XXIV. [D-asparagine, N-sulfonic acid],
XXV. [2β-carboxy, 3-carboxamido, propane-1-sulfonic acid],
XXVI. [2β-carboxy, 3-carboxamido, propane-1-sulfate],
XXVII. [1β-carboxy, 2-carboxamido, ethane sulfonic acid],
XXVIII. [1β-carboxy, 2-carboxamido, ethane sulfate],
XXIX. [D-asparagine, 3α-sulfonic acid],
XXX. [D-asparagine, 3α-sulfate],
XXXI. [D-asparagine, 3β-sulfonic acid],
XXXII. [D-asparagine, 3β-sulfate],

Yet another embodiment of the present invention, wherein said compound is selected from the group consisting of glutamic acid, glutamine and corresponding de-amino analogs:

I. [L-glutamic acid, N-sulfonic acid],
II. [2α,4-dicarboxy, butane-1-sulfonic acid],
III. [2α, 4-dicarboxy, butane-1-sulfate],
IV. [1α, 3-dicarboxy, propane sulfonic acid],
V. [1α, 3-dicarboxy, propane sulfate],
VI. [1β, 3-dicarboxy, propane sulfate],
VII. [1β, 3-dicarboxy, propane sulfonic acid],
VIII. [D-glutamic acid, N-sulfonic acid],
IX. [2β, 4-dicarboxy, butane-1-sulfonic acid],
X. [2β, 4-dicarboxy, butane-1-sulfate],
XI. [D-glutamic acid, 3α-sulfonic acid],

XII. [D-glutamic acid, 3α-sulfate],

XIII. [D-glutamic acid, 3β-sulfonic acid],

XIV. [D-glutamic acid, 3β-sulfate],

XV. [D-glutamic acid, 4α-sulfonic acid],

XVI. [D-glutamic acid, 4α-sulfate],

XVII. [D-glutamic acid, 4β-sulfonic acid],

XVIII. [D-glutamic acid, 3β-sulfate],

XIX. [L-glutamine, N-sulfonic acid],

XX. [2α-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XXI. [2α-carboxy, 4-carboxamido, butane-1-sulfate],

XXII. [1α-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXIII. [1α-carboxy, 3-carboxamido, propane-1-sulfate],

XXIV. [1β-carboxy, 3-carboxamido, propane-1-sulfate],

XXV. [1β-carboxy, 3-carboxamido, propane-1-sulfonic acid],

XXVI. [D-glutamine, N-sulfonic acid],

XXVII. [2β-carboxy, 4-carboxamido, butane-1-sulfonic acid],

XXVIII. [2β-carboxy, 4-carboxamido, butane-1-sulfate],

XXIX. [D-glutamine, 3α-sulfonic acid],

XXX. [D-glutamine, 3α-sulfate],

XXXI. [D-glutamine, 3β-sulfonic acid],

XXXII. [D-glutamine, 3β-sulfate],

XXXIII. [D-glutamine, 4α-sulfonic acid],

XXXIV. [D-glutamine, 4α-sulfate],

XXXV. [D-glutamine, 4β-sulfonic acid],

XXXVI. [D-glutamine, 4β-sulfate],

XXXVII. [L-homoglutamic acid, N-sulfonic acid],

XXXVIII. [Pentane-2α, 5-dicarboxy-1-sulfonic acid],

XXXIX. [Pentane-2α, 5-dicarboxy-1-sulfate],

XL. [Butane-1α, 4-dicarboxy-1-sulfonic acid],

XLI. [Butane-1α, 4-dicarboxy-1-sulfate],

Still another embodiment of the present invention, wherein said compound is selected from the group consisting of homoglutamic acid, homoglutamine and corresponding de-amino analogs:

I. [D-homoglutamic acid, N-sulfonic acid],
II. [Pentane-2β, 5-dicarboxy-1-sulfonic acid],
III. [Pentane-2β, 5-dicarboxy-1-sulfate],
IV. [Butane-1β, 4-dicarboxy-1-sulfonic acid],
V. [Butane-1β, 4-dicarboxy-1-sulfate],
VI. [D-homoglutamic acid, 3α-sulfonic acid],
VII. [D-homoglutamic acid, 3α-sulfate],
VIII. [D-homoglutamic acid, 3β-sulfonic acid],
IX. [D-homoglutamic acid, 3β-sulfate],
X. [D-homoglutamic acid, 4α-sulfonic acid],
XI. [D-homoglutamic acid, 4α-sulfate],
XII. [D-homoglutamic acid, 4β-sulfonic acid],
XIII. [D-homoglutamic acid, 4β-sulfate],
XIV. [D-homoglutamic acid, 5α-sulfate],
XV. [D-homoglutamic acid, 5α-sulfate],
XVI. [D-homoglutamic acid, 5β-sulfonic acid],
XVII. [D-homoglutamic acid, 5β-sulfate],
XVIII. [L-homoglutamine, N-sulfonic acid],
XIX. [Pentane-2α-carboxy, 5-carboxamido-1-sulfonic acid],
XX. [Pentane-2α-carboxy, 5-carboxamido-1-sulfate],
XXI. [Butane-1α-carboxy, 4-carboxamido-1-sulfonic acid],
XXII. [Butane-1α-carboxy, 4-carboxamido-1-sulfate],
XXIII. [D-homoglutamine, N-sulfonic acid],
XXIV. [Pentane-2β-carboxy, 5-carboxamido-1-sulfonic acid],
XXV. [Butane-1 β -carboxy, 4-carboxamido-1-sulfonic acid],
XXVI. [Butane-1 β -carboxy, 4-carboxamido-1-sulfate],
XXVII. [D-homoglutamine, 3α-sulfonic acid],

XXVIII. [D-homoglutamine, 3α-sulfate],

XXIX. [D-homoglutamine, 3β-sulfonic acid],

XXX. [D-homoglutamine, 3β-sulfate],

XXXI. [D-homoglutamine, 4α-sulfonic acid],

XXXII. [D-homoglutamine, 4α-sulfate],

XXXIII. [D-homoglutamine, 4β-sulfonic acid],

XXXIV. [D-homoglutamine, 4β-sulfate],

XXXV. [D-homoglutamine, 5α-sulfonic acid],

XXXVI. [D-homoglutamine, 5α-sulfate],

XXXVII. [D-homoglutamine, 5β-sulfonic acid] and

XXXVIII. [D-homoglutamine, 5β-sulfate].

Still another embodiment of a present invention relates to a compound incubation of BM leukocyte precursors with different concentrations of the synthetic compound increases the cell surface densities of CD11c, CD80, CD54 and CD11c to various levels with maximum up regulation at 200 mM.

Still further another embodiment of a present invention relates to a compound it gives the fold increase in the levels of molecules of cells stimulated with either 15 ng/ml of GM-CSF or 200 mM of the synthetic compound at 48 h of incubation.

Yet another embodiment of a present invention relates to a compound wherein the viability of the cultures is more than 99% at the end of the incubation period at this concentration of the synthetic compound.

Yet another embodiment of a present invention relates to a compound useful for inhibition of mononuclear TRAP- positive osteoclasts.

Yet another embodiment of a present invention relates to a compound useful for inhibition of fusion of mononuclear cells into multinuclear osteoclasts.

Yet another embodiment of a present invention relates to a compound useful for inhibition of bone resorption.

Yet another embodiment of a present invention relates to a compound has non-toxic to monocytes.

Yet another embodiment of a present invention relates to a compound has non- toxic to macrophages.

Further embodiment of a present invention relates to a method for inhibition of osteoclast formation comprising the step of administering a pharmaceutically acceptable amount of a compound to a subject in need thereof optionally with an additive, excipient, diluent or carrier.

Yet another embodiment of a present invention relates to a method wherein dosage the compound is 5 to 10 mg/ kg body weight

Yet another embodiment of a present invention relates to a method wherein the period of administration is 25-30 days.

Further embodiment of a present invention relates to a method for inhibition of mononuclear TRAP-positive osteoclasts comprising the step of administering a pharmaceutically acceptable amount of a compound subject in need thereof optionally with an additive, excipient, diluent or carrier.

Yet another embodiment of a present invention relates to a method wherein dosage of the compound is 5 to 10 mg / kg body weight

Yet another embodiment of a present invention relates to a method wherein the period of administration is 25–30 days.

Further embodiment of a present invention relates to a method for inhibition of multinuclear TRAP-positive osteoclasts comprising the step of administering a pharmaceutically acceptable amount of a compound to a subject in need thereof optionally with an additive, excipient, diluent or carrier.

Yet another embodiment of a present invention relates to a method wherein the dosage of the compound is 5 to 10 mg/ kg body weight.

Yet another embodiment of a present invention relates to a method wherein the period of administration is 5to 30 days.

Still further embodiment of a present invention relates to a method for modulation of immune response controlled by differentiation of dendricts cells comprising the step of administration a pharmaceutical acceptable amount of a compound to a subject in need thereof optionally with an additive, excipient , diluents or carrier.

Yet another embodiment of a present invention relates to a compound useful to induce differentiation of dendritic cells and modulation of immune response controlled by dendritic cell.

Yet another embodiment of a present invention relates to a compound useful in vaccine formulation to prevent more efficicent and faster presentation of antigens to T-cells thereby initiate primary protective Th1 immune response and help in the clearance of the pathogen. The compounds for differentiation of dendritic cells also contained different divalent metal ions such as Mg, Ca and Zn. The composition consisted of varying amounts of the above acid amino acid / dicarboxylic acid derivatives and their pharmaceutically acceptable salts. Non toxic salts of the present invention are contained all pharmaceutically acceptable salts, for example, general salts, acid addition salt, hydrate salts.

The compounds of the formulae (Ia), (Ib) and (Ic) of the present invention may be converted into the corresponding salts. Non toxic and water soluble salts are preferable. Suitable salts for example are as follows:

- Salts of alkaline earth metals (Mg, Ca etc)
- Ammonium Salts
- Salts of pharmaceutically acceptable organic amines (tetramethyl ammonium, triethyl amine, methyl amine, cyclopentyl amine, benzylamine, phenethylamine, piperidine, monoethanolamine, diethanolamine, tris(hydroxymethyl) amine, lysine, arginine, N-methyl glucamine, etc.

a) a process for the preparation of sulfonic acid / sulfate derivatives of the formula (Ia) (Ib) (Ic) and non-toxic salts thereof:

b) a process for the preparation of sulfonic acid / sulfate derivatives of the formula and non-toxic salts thereof:

c) a process for the preparation of sulfonic acid / sulfate derivatives of the formula) and non-toxic salts thereof:

d) In the compound of the present invention of the formula (Ia) wherein the compound is selected from the group consisting of aspartic acid, asparagine and corresponding de-amino analogs:

e) In the compound of the present invention of the formula (Ib) wherein the compound is selected from the group consisting of glutamic acid, glutamine and corresponding de-amino analogs:

f) In the compound of the present invention of the formula (Ic) wherein the compound is selected from the group consisting of homoglutamic acid, homoglutamine and corresponding de-amino analogs:

Among the various Antigen Presenting Cells (APCs) of the immune system, Dendritic Cells (DCs) constitute the most potent APCs and act as a bridge between the innate and the acquired arm of the immune system. This is largely attributed to the ability of DCs to take-up pico- to femtomoles of antigen and to stimulate primary naïve quiescent T cells, thereby initiating a primary immune response. DCs exist in various states of activation that translates into distinct functions. For example, DCs arising from the Bone Marrow (BM) are essentially immature DCs. These DCs exhibit low levels of T cell costimulatory molecules such as CD80, CD86, CD40 & CD54 and also low levels of surface MHC class I and class II molecules. Further, these DCs express a range of phagocytic, endocytic and scavenger receptors and owing to the above features are thus programmed for antigen capture and uptake. Upon contact with various inflammatory stimuli such as, TNF-□, bacterial endotoxins (e.g. LPS), CD40 ligand (CD40l), CpG containing bacterial DNA, double stranded viruses and certain (but not all) antigens, DCs undergo a process of maturation, wherein they now upregulate their surface levels of costimulatory molecules and MHC-peptide complexes (now exported to the cell surface following degradation and loading onto MHC trimers) and are thus programmed for antigen presentation and T lymphocyte stimulation. The transformation from the immature to the mature stage is a tightly regulated process often requiring T cell help. During maturation these DCs also secrete a range of cytokines such as TNF-□, IL-12, IFN-□ and low levels of IL-10. Owing to secretion of pro-inflammatory cytokines, DCs are thought to drive pro-inflammatory or Th1 responses and help in the clearance of the pathogen. Therefore, factors/molecules that increase the population of immature DCs in the immune system offer added advantage for the host's fight against infectious pathogens. In this context efforts have been focused on finding and generating ways to increase the DC numbers in

the immune system. These have included the use of recombinant DCs or even pathogens that have been transformed to express Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF), the growth factor that is conventionally used to generate DCs in vitro.

A number of studies have identified pathogen and host products such as proteins that induce the maturation of different DC subsets. Owing to their fully mature status these DCs are more programmed for antigen presentation and T cell stimulation and have reduced capacity to capture antigens of pathogens. Immature DCs that are de novo differentiated from precursors offer better advantage than mature DCs because of their ability to scavenge pathogens followed by their uptake and processing and subsequent presentation to T lymphocytes. Our observation on the ability of 'the molecule' to induce differentiation of Dendritic Cells from mouse bone marrow leukocyte precursors, therefore, assumes paramount importance and is a significant step towards modulation of immune responses controlled by DCs. As the DCs differentiated by 'the molecule' are immature in nature and resemble very closely to the DCs differentiated by GM-CSF they will be efficient not only at antigen capture but also be effective T cell stimulators.

Among the many applications, the two most important ones would include the use of 'the molecule' in vaccine formulations or in protection based studies that would promote more efficient and faster presentation of the antigens to T cells thereby initiate primary protective Th1 immune responses and help in the clearance of the pathogen. Further, 'the molecule' offers a cheap alternative to GM-CSF for commercial purposes to generate DCs in vitro for research based studies.

Basically, immuno-supression is a common clinical feature in many infectious diseases. This immuno-supression cripples the ability of the immune systems to get rid of the infectious agents eventuating in the death of the host. It has been found that the host recovering from disease after chemotherapy shows a significant improvement of antigen-specific immune functions. Despite the urgency of the need, and immuno-potentiator which can be of human use remains awaited. The cumulative incidence of the diseases obviates the need for a drug(s) that restores the immune response of the affected individual to a normal level.

In response to any invasion by a pathogen, the complex multicellular organisms have

evolved a defense mechanism to make their internal environment more hostile to invaders. All immune systems have one feature in common: they respond to infection by switching from a resting to an active state. The innate response limits the infection and activates Antigen Presenting Cells (APCs) to trigger adaptive immunity, which increases specificity and generates memory. Consequently, the immune responses that occur during an encounter with antigens-be it infectious agents or allergens are primarily characterized by the plasticity of their nature and magnitude. This feature provides an important advantage that permits the immune system to tailor its defense strategy to particular groups of antigens. Interactions between APCs such as **D**endritic cells (DCs) and macrophages and the different subsets of T cells ($CD4^+$ and $CD8^+$) in the T cell rich areas of the lymph nodes and spleen, amplify the consequent immune responses. Following this interaction, T helper (Th) cell precursors then differentiate into effectors. that secrete either pro-inflammatory or suppressor/regulatory cytokines such as Interferon (IFN)-□ Tumor Necrosis Factor (TNF)-□, and Interleukin (IL)-1, or IL-4, IL-10 and Transforming Growth Factor (TGF)-□, respectively.

Among the most potent of the APCs are the macrophages and different subsets of DCs, that together virtually regulate the antigen capture and presentation of the innate arm of the immune system. DCs are professional APCs that are continuously produced by the stem cells in the hematopoeitic tissues. DCs exist at various states of activation that are primarily classified as immature (iDCs) and mature (mDCs). iDCs are programmed for antigen capture, which upon contact with various stimuli, such as bacterial products, CD40 ligand, (TNF)-□, and certain antigens undergo a process of maturation wherein they now become programmed for antigen presentation and T-cell stimulation. Consequently, agents that promote the maturation of iDCs play a vital role in shaping the early immune responses elicited during an infection. Along with macrophages, that constitute the all important phagocytic component of the innate immune system DCs activate the effector cells such as the various subsets of T-cells, Natural Killer (NK) cells and NK-T cells by secreting a profile of cytokines that would eventually prime these effector cells to carryout their functions. These range from stimulating the adaptive arm of the immune system for the generation of antibody mediated responses, to stimulation of the cytotoxic activity by

the $CD8^+$ T-cells against the infected cells/tissues. The invention may provide a novel compound that will be useful in vaccination, cancer therapy and other immunomodulatory regiments.

The preferable specific compounds of the formulae (Ia), (Ib) and (Ic) are the derivatives of aspartic acid, asparagine and corresponding de-amino analogs (Table 1), glutamic acid, glutamine and corresponding de-amino analogs (Table 2) and homoglutamic acid, homoglutamine and corresponding de-amino analogs (Table 3) and non toxic salts thereof and example compounds.

BRIEF DESCRIPTION OF DRAWINGS:

Fig. 1, or Plate A represents surface level of CD 80.

Fig. 2, or Plate B, represents surface level of CD 54.

Fig. 3, or Plate C, represents surface level of CD 11c.

Fig. 4, or Plate D, represents surface level of CD H-2D (MHC class 1).

Fig. 5 -- Effect of compound as given in example 3 on RANKL-induced osteoclast differentiation from haemopoietic precursors of monocytes/macrophage lineage. Mice osteoclast precursors were incubated in the presence of M-CSF and RANKL in the absence and presence of the compound. Photomicrographs showing TRAP-positive osteoclasts in the absence (Fig. 5A) and presence (Fig. 5B) of the compound. This compound significantly inhibited osteoclast formation.

Fig. 6 -- Effect of compound as described in example 4 on RANKL-induced osteoclast differentiation from haemopoietic precursors of monocytes/macrophage lineage. Photomicrographs showing TRAP-positive osteoclasts induced by M-CSF and RANKL in the absence (Fig. 6A) and presence (Fig. 6B) of compound. This compound showed no inhibitory effect on osteoclast differentiation.

BRIEF DESCRIPTION OF THE ACCOMPANYING PLATES

Plate 1. Compound 1 induces differentiation of dendritic cells from BALB/c mouse bone marrow

Enriched leukocyte precursors from 4 to 6 weeks old mice were stimulated with varying concentrations of compound as given in example-3 for 48 h. Cells were stained for the surface levels of indicated markers. Plates A-D represent surface levels of CD80, CD54, CD11c and H-2D (MHC class I), respectively. Results obtained with Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) are also shown for comparison. Panels a to d in each Plate shows the surface levels of indicated markers on cells stimulated with 15 ng/ml of GM-CSF, 10 μg/ml, 5 μg /ml and 1 μg /ml of compound 1, respectively. The Green line represents staining of stimulated cells while the black line depicts staining of unstimulated cells.

Differentiation of *Dendritic cells*

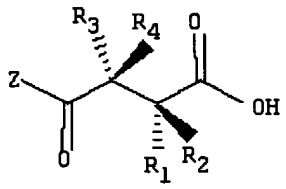
The fine suspension obtained above was transferred into a 50 ml sterile centrifuge tube and centrifuged for 10 minutes at 1200 rpm. After removing the supernatant, RBC lysis buffer was added, mixed thoroughly and incubated for 3-5 minutes at room temperature. The pellets were washed using HBSS wash buffer and then centrifuged again for 10 minutes at 1200 rpm. This process was repeated for one more time. The pellet was dissolved in 2 ml HBSS and passed through a pre-separation filter (Miltenyi Biotech # 130-041-407) to remove unwanted tissue etc. Microbeads (I-A, CD45R and CD90) were added to this clear solution and incubated for one hour at 4°C with shaking to eliminate other lymphocytes and macrophages and MHC positive cells. This suspension was then finally passed through a MACS (Magnetic Activated Cell Sorting) column to get essentially and predominately leukocyte precursors. The cell pellet was suspended in complete medium (RPMI 1640, 10% Foetal Calf Serum, Sodium pyruvate (1 mM) and 2-Mercaptoethanol (50 mM). About 2.5-3 x 10^6 leukocyte precursors were plated in each well of a 24 well culture plate in 1ml culture volume. Cells were stimulated with either 15 ng per ml of Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) or 50 micro gram per ml of the compound (neutralized with 1 M Tris HCl to achieve a pH of 7.0). The plate was incubated for 48 hours at 37°C in a CO_2 incubator.

Evaluation of cell surface marker expression

In order to evaluate the upregulation of various cell surface markers associated with Dendritic cells, flow cytometry on the cells stimulated with GM-CSF or the compound was carried out using fluorescent labeled antibodies to various molecules (CD11c, I-A^d, CD80, CD86, H2-D^d, CD54, CD40).

LIST OF TABLES

Table 1



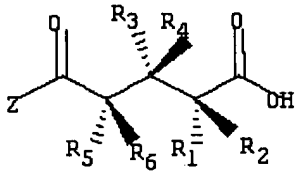
Structure 1

1. L- Aspartic acid, N-Sulfonic acid Z=OH, R_1=$NHSO_3H$, R_2=R_3=R_4=H
2. L-Aspartic acid, 2β-sulfonic acid Z=OH, R_1=NH_2, R_3=R_4=H, R_2=SO_3H
3. L-Aspartic acid, 2β-sulfate Z=OH, R_1=NH_2, R_3=R_4=H, R_2=OSO_3H
4. L-aspartic acid, 3α -sulfonic acid Z=OH, R_1=NH_2, R_2=R_4=H, R_3=SO_3H
5. L-aspartic acid, 3α-sulfate Z=OH, R_1=NH_2, R_2=R_4=H, R_3=OSO_3H
6. L-aspartic acid, 3β-sulfonic acid Z=OH, R_1=NH_2, R_2=R_3=H, R_4=SO_3H
7. L-aspartic acid, 3β-sulfate Z=OH, R_1=NH_2, R_2=R_3=H, R_4=OSO_3H
8. 2α, 3-dicarboxy, propane-1-sulfonic acid Z=OH,R_1=R_3=R_4=H, R_2=CH_2SO_3H
9. 2α,3-dicarboxy, propane-1-sulfate Z=OH, R_1=R_3=R_4=H, R_2=CH_2OSO_3H
10. 1α,2-carboxy ethane sulfonic acid Z=OH, R_1=R_3=R_4=H, R_2=SO_3H
11. 1α,2-carboxy ethane sulfate Z=OH, R_1=R_3=R_4=H, R_2=OSO_3H

12. D-aspartic acid, N-sulfonic acid Z=OH, R_2=$NHSO_3H$, R_1=R_3=R_4=H
13. 2β,3-carboxy,propane-1-sulfonic acid Z=OH, R_2=H, R_1=CH_2SO_3H
14. 2β,3-carboxy,propane-1-sulfate Z=OH, R_2=H, R_1=CH_2OSO_3H
15. 1β,2-carboxy ethane-1-sulfonic acid Z=OH, R_2=H, R_1=SO_3H
16. 1β,2-carboxy ethane-1-sulfate Z=OH, R_2=H, R_1=OSO_3H
17. D-aspartic acid, 2α-sulfonic acid Z=OH, R_2=NH_2, R_3=R_4=H, R_1=SO_3H
18. D-aspartic acid, 2α -sulfonic acid Z=OH, R_2=NH_2, R_3=R_4=H, R_1=SO_3H
19. D-Aspartic acid, 3α -sulfonic acid Z=OH, R_2=NH_2, R_1=R_4=H, R_3=SO_3H
20. D-Aspartic acid, 3α-sulfate Z=OH, R_2=NH_2, R_1=R_4=H, R_3=OSO_3H
21. D-Aspartic acid, 3β-sulfonic acid Z=OH, R_2=NH_2, R_1=R_3=H, R_4=SO_3H
22. D-aspartic acid, 3β-sulfate Z=OH, R_2=NH_2, R_1=R_3=H, R_4=OSO_3H
23. L-asparagine,N-sulfonic acid Z=NH_2, R_1=$NHSO_3H$, R_2=R_3=R_4=H
24. 2α-carboxy, 3-carboxamido, propane-1-sulfonic acid Z=NH_2, R_1=H, R_2=CH_2SO_3H
25. 2α-carboxy, 3-carboxamido, propane-1-sulfate Z=NH_2, R_1=H, R_2=CH_2OSO_3H
26. 1α-carboxy, 2-carboxamido, ethane sulfonic acid Z=NH_2, R_1=H, R_2=SO_3H
27. 1α-carboxy, 2-carboxamido, ethane sulfateZ=NH_2, R_1=H, R_2=OSO_3H
28. L-asparagine, 2β-sulfonic acid Z=R_1=NH_2, R_2=R_4=H, R_2=SO_3H
29. L-asparagine, 2β-sulfateZ=R_1=NH_2, R_2=R_4=H, R_3=OSO_3H
30. L-asparagine, 3α-sulfonic acid Z=R_1=NH_2, R_2=R_4=H, R_3=SO_3H
31. L-asparagine, 3α-sulfateZ=R_1=NH_2, R_2=R_4=H, R_3=OSO_3H
32. L-asparagine, 3β-sulfonic acid Z=R_1=NH_2, R_2=R_3=H, R_4=SO_3H
33. L-asparagine, 3β-sulfateZ=R_1=NH_2, R_2=R_3=H, R_4=OSO_3H
34. D-asparagine, N-sulfonic acid Z=NH_2, R_2=$NHSO_3H$, R_1=R_3=R_4=H
35. 2β-carboxy, 3-carboxamido, propane-1-sulfonic acidZ=NH_2, R_2 to R_4=H, R_1=CH_2SO_3H
36. 2β-carboxy, 3-carboxamido, propane-1-sulfateZ=NH_2, R_2 to R_4=H,R_1=CH_2SO_3H

37. 1β-carboxy, 2-carboxamido, ethane sulfonic acid]Z=OH, R_2 to R_4=H, R_1=SO_3H
38. 1β-carboxy, 2-carboxamido, ethane sulfate Z=OH, R_2 to R_4=H, R_1=OSO_3H
39. D-asparagine, 2α-sulfonic acid Z=R_2=NH_2, R_3=R_4=H, R_1=SO_3H
40. D-asparagine, 2α-sulfateZ=R_2=NH_2, R_3=R_4=H, R_1=OSO_3H
41. D-asparagine, 3α-sulfonic acid Z=R_2=NH_2, R_1=R_4=H, R_3=SO_3H
42. D-asparagine, 3α-sulfateZ=R_2=NH_2, R_1=R_4=H, R_3=OSO_3H
43. D-asparagine, 3β-sulfonic acid Z=R_2=NH_2, R_1=R_3=H, R_4=SO_3H
44. D-asparagine, 3β-sulfateZ=R_2=NH_2, R_1=R_3=H, R_4=OSO_3H

Table 2



Structure 2

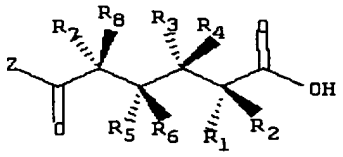
1. L-glutamic acid, N-sulfonic acid Z=OH, R_1=$NHSO_3H$, R_2=R_3=R_4=R_5=R_6=H
2. 2α, 4-dicarboxy, butane-1-sulfonic acid Z=OH, R_1, R_3 to R_6=H, R_2=CH_2SO_3H
3. 2α, 4-dicarboxy, butane-1-sulfate Z=OH, R_1, R_3 to R_6=H, R_2=CH_2OSO_3H
4. 1α, 3-dicarboxy, propane sulfonic acid Z=OH, R_1, R_3 to R_6=H, R_2=SO_3H
5. 1α, 3-dicarboxy, propane sulfate Z=OH, R_1, R_3 to R_6=H, R_2=OSO_3H
6. 1β, 3-dicarboxy, propane sulfate Z=OH, R_2 to R_6=H, R_1=OSO_3H
7. 1β, 3-dicarboxy, propane sulfonic acid Z=OH, R_2 to R_6=H, R_1=SO_3H
8. L-glutamic acid, 2β-sulfonic acid Z=OH, R_1=NH_2, R_3 to R_6=H, R_2=SO_3H
9. L-glutamic acid, 2β-sulfateZ=OH, R_1=NH_2, R_3 to R_6=H, R_2=OSO_3H

10. L-glutamic acid, 3α-sulfonic acid Z=OH, R_1=NH_2, R_2=H, R_4 to R_6=H, R_3=SO_3H
11. L-glutamic acid, 3α-sulfate Z=OH, R_1=NH_2, R_2=H, R_4 to R_6=H, R_3=OSO_3H
12. L-glutamic acid, 3β-sulfonic acid Z=OH, R_1=NH_2, R_2=R_3=R_5=R_6=H, R_4=SO_3H
13. L-glutamic acid, 3β-sulfate Z=OH, R_1=NH_2, R_2=R_3=R_5=R_6=H, R_4=OSO_3H
14. L-glutamic acid, 4α-sulfonic acid Z=OH, R_1=NH_2, R_2=R_3=R_4=R_6=H, R_5=SO_3H
15. L-glutamic acid, 4α-sulfate Z=OH, R_1=NH_2, R_2=R_3=R_4=R_6=H, R_5=OSO_3H
16. L-glutamic acid, 4β-sulfonic acid Z=OH, R_1=NH_2, R_2 to R_5=H, R_6=SO_3H
17. L-glutamic acid, 4β-sulfate Z=OH, R_1=NH_2, R_2 to R_5=H, R_6=OSO_3H
18. D-glutamic acid, N-sulfonic acidZ=OH, R_2=$NHSO_3H$, R_1, R_3 to R_6=H
19. 2β, 4-dicarboxy, butane-1-sulfonic acid Z=OH, R_2 to R_6=H, R_1=CH_2SO_3H
20. 2β, 4-dicarboxy, butane-1-sulfate Z=OH, R_2 to R_6=H, R_1=CH_2OSO_3H
21. D-glutamic acid, 2α-sulfonic acid Z=OH, R_2=NH_2, R_3 to R_6 H, R_1=SO_3H
22. D-glutamic acid, 2α-sulfate Z=OH, R_2=NH_2, R_3 to R_6 H, R_1=OSO_3H
23. D-glutamic acid, 3α-sulfonic acid Z=OH, R_2=NH_2, R_1, R_4 to R_6 H, R_3=SO_3H
24. D-glutamic acid, 3α-sulfate Z=OH, R_2=NH_2, R_1, R_4 to R_6 H, R_3=OSO_3H
25. D-glutamic acid, 3β-sulfonic acid Z=OH, R_2=NH_2, R_1=R_3=R_5=R_6=H, R_4=SO_3H
26. D-glutamic acid, 3β-sulfate Z=OH, R_2=NH_2, R_1=R_3=R_5=R_6=H, R_4=OSO_3H
27. D-glutamic acid, 4α-sulfonic acid Z=OH, R_2=NH_2, R_1=R_3=R_4=R_6=H, R_5=SO_3H
28. D-glutamic acid, 4α-sulfate Z=OH, R_2=NH_2, R_1=R_3=R_4=R_6=H, R_5=OSO_3H
29. D-glutamic acid, 4β-sulfonic acid Z=OH, R_2=NH_2, R_1=R_3=R_4=R_5=H, R_6=SO_3H
30. D-glutamic acid, 4β-sulfate Z=OH, R_2=NH_2, R_1=R_3=R_4=R_5=H, R_6=OSO_3H
31. L-glutamine, N-sulfonic acid Z=NH_2, R_1=$NHSO_3H$, R_2 to R_6=H

32. L-glutamine, 2β-sulfonic acid $Z=R_1=NH_2$, R_3 to $R_6=H$, $R_2=SO_3H$
33. L-glutamine, 2β-sulfate $Z=R_1=NH_2$, R_3 to $R_6=H$, $R_2=OSO_3H$
34. L-glutamine, 3α-sulfonic acid $Z=R_1=NH_2$, $R_2=H$, R_3 to $R_6=H$, $R_3=SO_3H$
35. L-glutamine, 3α-sulfate $Z=R_1=NH_2$, $R_2=H$, R_3 to $R_6=H$, $R_3=OSO_3H$
36. L-glutamine, 3β-sulfonic acid $Z=R_1=NH_2$, $R_2=R_3=R_5=R_6=H$, $R_4=SO_3H$
37. L-glutamine, 3β-sulfate $Z=R_1=NH_2$, $R_2=R_3=R_5=R_6=H$, $R_4=OSO_3H$
38. L-glutamine, 4α-sulfonic acid $Z=R_1=NH_2$, $R_2=R_3=R_4=R_6=H$, $R_5=SO_3H$
39. L-glutamine, 4α-sulfate $Z=R_1=NH_2$, $R_2=R_3=R_4=R_6=H$, $R_5=OSO_3H$
40. L-glutamine, 4β-sulfonic acid $Z=R_1=NH_2$, R_2 to $R_5=H$, $R_6=SO_3H$
41. L-glutamine, 4β-sulfate $Z=R_1=NH_2$, R_2 to $R_5=H$, $R_6=OSO_3H$
42. 2α-carboxy, 4-carboxamido, butane-1-sulfonic acid $Z=NH_2$, R_1, R_3 to $R_6=H$, $R_2=CH_2SO_3H$
43. 2α-carboxy, 4-carboxamido, butane-1-sulfate $Z=NH_2$, R_1, R_3 to $R_6=H$, $R_2=CH_2OSO_3H$
44. 1α-carboxy, 3-carboxamido, propane-1-sulfonic acid $Z= NH_2$, R_1, R_3 to $R_6=H$, $R_2=SO_3H$
45. 1α-carboxy, 3-carboxamido, propane-1-sulfate $Z= NH_2$, R_1, R_3 to $R_6=H$, $R_2=OSO_3H$
46. 1β-carboxy, 3-carboxamido, propane-1-sulfate $Z= NH_2$, R_2 to $R_6=H$, $R_1=OSO_3H$
47. 1β-carboxy, 3-carboxamido, propane-1-sulfonic acid $Z= NH_2$, R_2 to $R_6=H$, $R_1=SO_3H$
48. D-glutamine, N-sulfonic acid $Z=NH_2$, $R_2=NHSO_3H$; $R_1=H$, R_3 to $R_6=H$
49. 2β-carboxy, 4-carboxamido, butane-1-sulfonic acid $Z= NH_2$, R_2 to $R_6=H$, $R_1=CH_2SO_3H$
50. 2β-carboxy, 4-carboxamido, butane-1-sulfate $Z= NH_2$, R_2 to $R_6=H$, $R_1=CH_2OSO_3H$
51. D-glutamine, 2α-sulfonic acid $Z= NH_2$, $R_2=NH_2$, R_3 to $R_6=H$, $R_1=SO_3H$
52. D-glutamine, 2α-sulfate $Z=NH_2$, $R_2=NH_2$, R_3 to $R_6=H$, $R_1=OSO_3H$
53. D-glutamine, 3α-sulfonic acid $Z=NH_2$, $R_2=NH_2$, R_1, R_4 to R_6 H, $R_3=SO_3H$

54. D-glutamine, 3α-sulfate Z=R_2=NH_2, R_1, R_4 to R_6 H, R_3=OSO_3H
55. D-glutamine, 3β-sulfonic acid Z=R_2=NH_2, R_1=R_3=R_5=R_6=H, R_4=SO_3H
56. D-glutamine, 3β-sulfate Z=R_2=NH_2, R_1=R_3=R_5=R_6=H, R_4=OSO_3H
57. D-glutamine, 4α-sulfonic acid Z=R_2=NH_2, R_1=R_3=R_4=R_6=H, R_5=SO_3H
58. D-glutamine, 4α-sulfate Z=R_2=NH_2, R_1=R_3=R_4=R_6=H, R_5=OSO_3H
59. D-glutamine, 4β-sulfonic acid Z=R_2=NH_2, R_1=R_3=R_4=R_5=H, R_6=SO_3H
60. D-glutamine, 4β-sulfate Z=R_2=NH_2, R_1=R_3=R_4=R_5=H, R_6=OSO_3H

Table 3



structure 3

1. L-homoglutamic acid, N-sulfonic acid Z=OH, R_1=$NHSO_3H$, R_2 to R_8=H
2. Pentane-2α, 5-dicarboxy-1-sulfonic acid Z=OH, R_1, R_3 to R_8=H, R_2=CH_2SO_3H
3. Pentane-2α, 5-dicarboxy-1-sulfate Z=OH, R_1, R_3 to R_8=H, R_2=CH_2OSO_3H
4. Butane-1α, 4-dicarboxy-1-sulfonic acid Z= OH, R_1, R_3 to R_8=H, R_2=SO_3H
5. Butane-1α, 4-dicarboxy-1-sulfate Z=OH, R_1, R_3 to R_8=H, R_2=OSO_3H
6. L-homoglutamic acid, 2β-sulfonic acid Z=OH, R_1=NH_2, R_3 to R_8=H, R_2=SO_3H
7. L-homoglutamic acid, 2β-sulfate Z=OH, R_1=NH_2, R_3 to R_8=H, R_2=OSO_3H
8. L-homoglutamic acid, 3α-sulfonic acid Z=OH, R_1=NH_2, R_2=H, R_4 to R_8 H, R_3=SO_3H
9. L-homoglutamic acid, 3α-sulfate Z=OH, R_1=NH_2, R_2=H, R_4 to R_8 H, R_3=OSO_3H
10. L-homoglutamic acid, 3β-sulfonic acid Z=OH, R_1=NH_2, R_2=R_3=H, R_5 to R_8=H, R_4=SO_3H

11. L-homoglutamic acid, 3β-sulfate Z=OH, R_1=NH_2, R_2=R_3=H, R_5 to R_8=H, R_4=OSO_3H
12. L-homoglutamic acid, 4α-sulfonic acid Z=OH, R_1=NH_2, R_2=R_3=R_4=H, R_6 to R_8=H, R_5=SO_3H
13. L-homoglutamic acid, 4α-sulfate Z=OH, R_1=NH_2, R_2=R_3=R_4=H, R_6 to R_8=H, R_5=OSO_3H
14. L-homoglutamic acid, 4β-sulfonic acid Z=OH, R_1=NH_2, R_2=R_5=H, R_7=R_8=H, R_6=SO_3H
15. L-homoglutamic acid, 4β-sulfate Z=OH, R_1=NH_2, R_2=R_5=H, R_7=R_8=H, R_6=OSO_3H
16. L-homoglutamic acid, 5α-sulfonic acid Z=OH, R_1=NH_2, R_2 to R_6=H, R_8 =H, R_7=SO_3H
17. L-homoglutamic acid, 5α-sulfate Z=OH, R_1=NH_2, R_2 to R_6=H, R_8 =H, R_7=OSO_3H
18. L-homoglutamic acid, 5β-sulfonic acid Z=OH, R_1=NH_2, R_2 to R_7 =H, R_8=SO_3H
19. L-homoglutamic acid, 5β-sulfate Z=OH, R_1=NH_2, R_2 to R_7 =H, R_8=OSO_3H
20. D-homoglutamic acid, N-sulfonic acid Z=OH, R_2=$NHSO_3H$, R_1, R_3 to R_8=H
21. Pentane-2β, 5-dicarboxy-1-sulfonic acid Z=OH, R_2 to R_8=H, R_1=CH_2SO_3H
22. Pentane-2β, 5-dicarboxy-1-sulfate Z=OH, R_2 to R_8=H, R_1=CH_2OSO_3H
23. Butane-1β, 4-dicarboxy-1-sulfonic acid Z=OH, R_2 to R_8=H, R_1=SO_3H
24. Butane-1β, 4-dicarboxy-1-sulfate Z=OH, R_2 to R_8=H, R_1=OSO_3H
25. D-homoglutamic acid, 2α-sulfonic acid Z=OH, R_2=NH_2, R_3 to R_8=H, R_1=SO_3H
26. D-homoglutamic acid, 2α-sulfate Z=OH, R_2=NH_2, R_3 to R_8=H, R_1=OSO_3H
27. D-homoglutamic acid, 3α-sulfonic acid Z=OH, R_2=NH_2, R_1, R_4 to R_8 H, R_3=SO_3H

28. D-homoglutamic acid, 3α-sulfate Z=OH, R_2=NH_2, R_1, R_4 to R_8 H, R_3=OSO_3H
29. D-homoglutamic acid, 3β-sulfonic acid Z=OH, R_2=NH_2, R_1=R_3=H, R_5 to R_8=H, R_4=SO_3H
30. D-homoglutamic acid, 3β-sulfate Z=OH, R_2=NH_2, R_1=R_3=H, R_5 to R_8=H, R_4=OSO_3H
31. D-homoglutamic acid, 4α-sulfonic acid Z=OH, R_2=NH_2, R_1=R_3=R_4=H, R_6 to R_8=H, R_5=SO_3H
32. D-homoglutamic acid, 4α-sulfate Z=OH, R_2=NH_2, R_1=R_3=R_4=H, R_6 to R_8=H, R_5=OSO_3H
33. D-homoglutamic acid, 4β-sulfonic acid Z=OH, R_2=NH_2, R_1=H, R_3 to R_5=H, R_7=R_8=H, R_6=SO_3H
34. D-homoglutamic acid, 4β-sulfate Z=OH, R_2=NH_2, R_1=H, R_3 to R_5=H, R_7=R_8=H, R_6=OSO_3H
35. D-homoglutamic acid, 5α-sulfonic acid Z=OH, R_2=NH_2, R_1=R_8=H, R_3 to R_6=H, R_7=SO_3H
36. D-homoglutamic acid, 5α-sulfate Z=OH, R_2=NH_2, R_1=R_8=H, R_3 to R_6=H, R_7=OSO_3H
37. D-homoglutamic acid, 5β-sulfonic acid Z=OH, R_2=NH_2, R_1=H, R_3 to R_7=H, R_8=SO_3H
38. D-homoglutamic acid, 5β-sulfate Z=OH, R_2=NH_2, R_1=H, R_3 to R_7=H, R_8=OSO_3H
39. L-homoglutamine, N-sulfonic acid Z=NH_2, R_1=$NHSO_3H$, R_2 to R_8=H
40. Pentane-2α-carboxy, 5-carboxamido-1-sulfonic acid Z=NH_2, R_1 and R_3 to R_8=H, R_2=CH_2SO_3H
41. Pentane-2α-carboxy, 5-carboxamido-1-sulfate Z=NH_2, R_1 and R_3 to R_8=H, R_2=CH_2OSO_3H
42. Butane-1α-carboxy, 4-carboxamido-1-sulfonic acid Z=NH_2, R_1 and R_3 to R_8=H, R_2=SO_3H

43. Butane-1α-carboxy, 4-carboxamido-1-sulfate Z=NH_2, R_1 and R_3 to R_8=H, R_2=OSO_3H
44. L-homoglutamine, 2β-sulfonic acid Z=R_1=NH_2, R_3 to R_8=H, R_2=SO_3H
45. L-homoglutamine, 2β-sulfate Z=R_1=NH_2, R_3 to R_8=H, R_2=OSO_3H
46. L-homoglutamine, 3α-sulfonic acid Z=R_1=NH_2, R_2=H, R_4 to R_8=H, R_3=SO_3H
47. L-homoglutamine, 3α-sulfateZ=R_1=NH_2, R_2=H, R_4 to R_8=H, R_3=OSO_3H
48. L-homoglutamine, 3β-sulfonic acid Z=R_1=NH_2, R_2=R_3=H, R_5 to R_8=H, R_4=SO_3H
49. L-homoglutamine, 3β-sulfate Z=R_1=NH_2, R_2=R_3=H, R_5 to R_8=H, R_4=OSO_3H
50. L-homoglutamine, 4α-sulfonic acid Z=R_1=NH_2, R_2=R_3=R_4=H, R_6 to R_8=H, R_5=SO_3H
51. L-homoglutamine, 4α-sulfate Z=R_1=NH_2, R_2=R_3=R_4=H, R_6 to R_8=H, R_5=OSO_3H
52. L-homoglutamine, 4β-sulfonic acid Z=R_1=NH_2, R_2=R_5=H, R_7=R_8=H, R_6=SO_3H
53. L-homoglutamine, 4β-sulfate Z=R_1=NH_2, R_2=R_5=H, R_7=R_8=H, R_6=OSO_3H
54. L-homoglutamine, 5α-sulfonic acid Z=R_1=NH_2, R_2 to R_6=H, R_8=H, R_7=SO_3H
55. L-homoglutamine, 5α-sulfate Z=R_1=NH_2, R_2 to R_6=H, R_8=H, R_7=OSO_3H
56. L-homoglutamine, 5β-sulfonic acid Z=R_1=NH_2, R_2 to R_7=H, R_8=SO_3H
57. L-homoglutamine, 5β-sulfate Z=R_1=NH_2, R_2 to R_7=H, R_8=OSO_3H
58. D-homoglutamine, N-sulfonic acid Z=NH_2, R_2=$NHSO_3H$, R_1 and R_3 to R_8=H
59. Pentane-2β-carboxy, 5-carboxamido-1-sulfonic acid Z=NH_2, R_2 to R_8=H, R_1=CH_2SO_3H
60. Pentane-2β-carboxy, 5-carboxamido-1-sulfate Z=NH_2, R_2 to R_8=H, R_1=CH_2OSO_3H

61. Butane-1 β -carboxy, 4-carboxamido-1-sulfonic acid $Z=NH_2$, R_2 to $R_8=H$, $R_1=SO_3H$
62. Butane-1 β -carboxy, 4-carboxamido-1-sulfate $Z=NH_2$, R_2 to $R_8=H$, $R_1=OSO_3H$
63. D-homoglutamine, 2α-sulfonic acid $Z=R_2=NH_2$, R_3 to R_8 H, $R_1=SO_3H$
64. D-homoglutamine, 2α-sulfate $Z=R_2=NH_2$, R_3 to R_8 H, $R_1=OSO_3H$
65. D-homoglutamine, 3α-sulfonic acid $Z=R_2=NH_2$, R_1, R_4 to R_8 H, $R_3=SO_3H$
66. D-homoglutamine, 3α-sulfate $Z=R_2=NH_2$, R_1, R_4 to R_8 H, $R_3=OSO_3H$
67. D-homoglutamine, 3β-sulfonic acid $Z=R_2=NH_2$, $R_1=R_3=H$, R_5 to $R_8=H$, $R_4=SO_3H$
68. D-homoglutamine, 3β-sulfate $Z=R_2=NH_2$, $R_1=R_3=H$, R_5 to $R_8=H$, $R_4=OSO_3H$
69. D-homoglutamine, 4α-sulfonic acid $Z=R_2=NH_2$, $R_1=R_3=R_4=H$, R_6 to $R_8=H$, $R_5=SO_3H$
70. D-homoglutamine, 4α-sulfate $Z=R_2=NH_2$, $R_1=R_3=R_4=H$, R_6 to $R_8=H$, $R_5=OSO_3H$
71. D-homoglutamine, 4β-sulfonic acid $Z=R_2=NH_2$, $R_1=H$, R_3 to $R_5=H$, $R_7=R_8=H$, $R_6=SO_3H$
72. D-homoglutamine, 4β-sulfate $Z=R_2=NH_2$, $R_1=H$, R_3 to $R_5=H$, $R_7=R_8=H$, $R_6=OSO_3H$
73. D-homoglutamine, 5α-sulfonic acid $Z=R_2=NH_2$, $R_1=R_8=H$, R_3 to R_6 =H, $R_7=SO_3H$
74. D-homoglutamine, 5α-sulfate $Z=R_2=NH_2$, $R_1=R_8=H$, R_3 to $R_6=H$, $R_7=OSO_3H$
75. D-homoglutamine, 5β-sulfonic acid $Z=R_2=NH_2$, $R_1=H$, R_3 to $R_7=H$, $R_8=SO_3H$
76. D-homoglutamine, 5β-sulfate $Z=R_2=NH_2$, $R_1=H$, R_3 to $R_7=H$, $R_8=OSO_3H$

EXAMPLES:

The following reference example and examples illustrate the present invention but do not limit the present invention.

The solvents in the parenthesis show the developing and eluting solvents and the ratios of the solvent used are by volume in the chromatographic separation or TLC.

The solvents in the parenthesis in NMR show the solvents used in measurement.

Reference example 1

L-glutamyl, N-sulfonic acid from glutamic acid mono tertiary butyl ester

Glutamic acid monotertiary butyl ester (1 eq.) was added portion-wise to a solution of SO_2Cl_2 (2 eq.) in dry CH_2Cl_2 at 0°C followed by Et_3N (3 eq.). Resulting solution stirred for 8 hrs at r. t. when TLC showed complete consumption of starting material. Solvent was evaporated and the crude was dried in vacuum. 3 ml water was added to it and the slurry was stirred for 1 hr. To the slurry was added 45 ml CH_2Cl_2 followed by 3 eq of TFA at 0° C. The resulting solution was stirred at r. t. for 24 hrs. The solvent was evaporated and dried in vacuum. The pseudo molecular ion, $[M-H]^-$ at 226.0049 confirmed the structure of the product L-glutamyl, N-sulfonic acid (calculated for C5H8NO7S; 226.0026).

Reference example 2

L-glutamyl, N-sulfonic acid from glutamic acid di tertiary butyl ester

Glutamic acid ditertiary butyl ester (1 eq.) was added portion-wise to a solution of SO_2Cl_2 (2 eq.) in dry CH_2Cl_2 at 0°C followed by Et_3N (3 eq.). Resulting solution stirred for 8 hrs at r. t. when TLC showed complete consumption of starting material. Solvent was evaporated and the crude was dried in vacuum. 3 ml water was added to it and the slurry was stirred for 1 hr. To the slurry was added 45 ml CH_2Cl_2 followed by 3 eq of TFA at 0°C. The resulting solution was stirred at r. t. for 24 hrs. The solvent was evaporated and dried in vacuum. The pseudo molecular ion, $[M-H]^-$ at 226.0049 confirmed the structure of the product L-glutamyl, N-sulfonic acid (calculated for C5H8NO7S; 226.0026).

Reference example 3

L-Aspartyl, N-sulfonic acid from L-aspartic acid di tertiary butyl ester

L-aspartic acid di tertiary butyl ester (1 eq.) was added portion-wise to a solution of SO_2Cl_2 (2 eq.) in dry CH_2Cl_2 at 0°C followed by Et_3N (3 eq.). Resulting solution stirred for 8 hrs at r. t. when TLC showed complete consumption of starting material. Solvent was evaporated and the crude was dried in vacuum. 3 ml water was added to it and the slurry was stirred for 1 hr. To the slurry was added 45 ml CH_2Cl_2 followed by 3 eq of TFA at 0°C. The resulting solution was stirred at r. t. for 24 hrs. The solvent was evaporated and

dried in vacuum. The pseudo molecular ion, $[M-H]^-$ at 211.9885 confirmed the structure of the product L-aspartyl, N-sulfonic acid (calculated for C4H6NO7S; 211.9870).

Reference example 4

L-Homoglutamyl, N-sulfonic acid from L-Homoglutamic acid di tertiary butyl ester

L-Homoglutamic acid di tertiary butyl ester (1 eq.) was added portion-wise to a solution of SO_2Cl_2 (2 eq.) in dry CH_2Cl_2 at 0°C followed by Et_3N (3 eq.). Resulting solution stirred for 8 hrs at r. t. when TLC showed complete consumption of starting material. Solvent was evaporated and the crude was dried in vacuum. 3 ml water was added to it and the slurry was stirred for 1 hr. To the slurry was added 45 ml CH_2Cl_2 followed by 3 eq of TFA at 0°C. The resulting solution was stirred at r. t. for 24 hrs. The solvent was evaporated and dried in vacuum. The pseudo molecular ion, $[M-H]^-$ at 240.0169 confirmed the structure of the product L-Homoglutamyl, N-sulfonic acid (calculated for C6H10NO7S; 240.0182).

Reference example 5

The calcium salt of L-glutamyl-N-sulphonic acid was prepared by adding 1 M equivalent of $CaCl_2$ solution and incubated at temperature ranging from 30±5° C. The resulting complex was freeze-dried. The freeze-dried compound was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for dendritic celll differentiation (Table A).

Table A. Stimulation of BM precursors with the synthetic compound differentiates cells with DC specific markers.

Fold increase in Relative MFI over unstimulated control

	Surface markers				Viability
Group	CD80	CD54	H-2D^d	CD11c	% of Viable cells
GM-CSF	3.3	4.0	2.0	5.0	180
Compound	2.5	4.0	3.0	2.0	150

Table-A gives the fold increase in the levels of some of the molecules of cells stimulated with either 15 ng/ml of GM-CSF or 50 micro gram per ml of the synthetic compound at 48h of incubation over unstimulated controls. The viability of the cultures was more then

99% at the end of the incubation period at this concentration of the synthetic compound. The data suggests that 'the compound' induces the differentiation of DCs from BM precursors.

Reference example 6

The L-glutamyl-N-sulphonic acid prepared as described in Examples 1 & 2 was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for dendritic cell differentiation (Table B).

Reference example 7

The calcium salt of L-glutamic acid was prepared by adding 1 M equivalent of $CaCl_2$ solution and incubated at temperature ranging from 30 ± 5^{o} C. The resulting complex was freeze-dried. The freeze-dried compound was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for dendritic cell differentiation (Table B).

Reference example 8

The L-glutamic acid was reconstituted in sterilized distilled water and assessed in a ose-dependent manner for dendritic cell differentiation (Table B).

Table B: Stimulation of BM precursors with the synthetic compound differentiates cells with DC specific markers

Fold increase in Relative MFI over unstimulated control

	Surface markers				Viability
Group	CD80	CD54	H-2D^{d}	CD11c	% of Viable cells
GM-CSF	3.3	4.0	2.0	5.0	180
Example 6	1.5	2.0	1.2	1.0	115
Example 7	1.0	1.0	N.D.	1.0	90
Example 8	1.0	0.9	N.D.	1.1	95

Reference example 9

Isolation of *bone marrow*

For each set of experiment a group of 4 BALB/c mice were sacrificed by transferring the

animals in a chloroform chamber. The hind limbs of the mouse were removed carefully and placed in a Petri dish with HBSS (Hanks Balanced Saline Solution) wash buffer. The tibias and femurs were cleared of all surrounding and attached tissues. This was followed by chipping the ends of bones. The bone marrow was flushed out by injecting HBSS solution into the bone with the help of a hypodermal syringe (No. 26 gauge). The bone marrow was finally made into a fine suspension by syringing in and out of the fluid several times using an 18 gauge syringe needle.

Reference example 10

The calcium salt of L-glutamyl-N-sulphonic acid was prepared by adding 1 M equivalent of $CaCl_2$ solution and incubated at temperature ranging from $30\pm5^{\circ}$ C. The resulting complex was freeze-dried. The freeze-dried compound was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for inhibition of osteoclast differentiation (Table A).

Table A: Effect of compound 1 (L-glutamyl-N-sulphonic acid, Ca salt) on osteoclast formation

Culture conditions	**Number of TRAP-positive multinuclear cells/well of 96 well plate (Mean ± SEM)**	**% inhibition**
M-CSF	0	-
M-CSF + RANKL	138.00 ± 9.37	-
M-CSF + RANKL + compound 1 (0.5 µg/ml)	109.67 ± 9.79	21.01
M-CSF + RANKL + compound 1 (1.5 µg/ml)	52.17 ± 6.42	62.19
M-CSF + RANKL + compound 1 (3.0 µg/ml)	14.67 ± 1.98	89.36
M-CSF + RANKL + compound 1 (5.0 µg/ml)	2.83 ± 1.05	97.94

Culture of murine bone marrow cells in the presence of M-CSF and RANKL induces the formation of osteoclasts, which were detected as TRAP-positive cells. A dose dependent inhibition in the number of osteoclast cells generated as observed with increasing dose of compound 1. Values given are the mean ± SD of five separate experiments

Reference example 11

The calcium salt of L-glutamic acid was prepared by adding 1 M equivalent of $CaCl_2$ solution and incubated at temperature ranging from 30±5° C. The resulting complex was freeze-dried. The freeze-dried compound was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for inhibition of osteoclast differentiation (Table B).

Table B: Effect of L-glutamic acid, calcium salt on osteoclast formation

Culture conditions	**Number of TRAP-positive multinuclear cells/well of 96 well plate (Mean ± SEM)**	**% inhibition**
M-CSF	0	-
M-CSF + RANKL	158.33 ± 12.00	-
M-CSF + RANKL + compound 2 (0.5 µg/ml)	167.17 ± 7.95	0
M-CSF + RANKL + compound 2 (1.5 µg/ml)	152.83 ± 10.47	3.47
M-CSF + RANKL + compound 2 (3.0 µg/ml)	130.50 ± 13.57	17.37
M-CSF + RANKL + compound 2 (5.0 µg/ml)	119.50 ± 10.00	24.52

For detail see legend to example 5

Reference example 12

The L-glutamyl-N-sulphonic acid prepared as described in Examples 1 & 2 was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for inhibition of osteoclast differentiation (Table D).

Table -D: Effect of L-glutamyl-N-sulphonic acid on osteoclast formation

Culture conditions	**Number of TRAP-positive multinuclear cells/well of 96 well platè** **(Mean ± SEM)**	**% inhibition**
M-CSF	0	-
M-CSF + RANKL	146.83 ± 11.89	-
M-CSF + RANKL + compound 3 (0.5 µg/ml)	154.67 ± 8.43	0
M-CSF + RANKL + compound 3 (1.5 µg/ml)	150.33 ± 8.82	0
M-CSF + RANKL + compound 3 (3.0 µg/ml)	112.67 ± 8.63	23.23
M-CSF + RANKL + compound 3 (5.0 µg/ml)	110.00± 6.72	25.08

For detail see legend to example 5

Reference example 13

The L-glutamic acid was reconstituted in sterilized distilled water and assessed in a dose dependent manner for inhibition of osteoclast differentiation (Table E).

Table E: Effect of L-glutamic acid on osteoclast formation

Culture conditions	**Number of TRAP-positive multinuclear cells/well of 96 well plate (Mean ± SEM)**	**% inhibition**
M-CSF	0	-
M-CSF + RANKL	156.00 ± 12.26	0
M-CSF + RANKL + compound 4 (0.5 µg/ml)	173.33 ± 6.50	0
M-CSF + RANKL + compound 4 (1.5 µg/ml)	155.00± 8.23	0.64
M-CSF + RANKL + compound 4 (3.0 µg/ml)	145.83± 14.71	7.05
M-CSF + RANKL + compound 4 (5.0 µg/ml)	112.67± 10.74	27.77

For detail see legend to example 5

Reference example 14

The L-Aspartic acid, N-sulphonic acid as prepared in example 3 was mixed with 1 M equivalent of $CaCl_2$ solution and incubated at temperature ranging from 30±5° C. The resulting complex was freeze-dried. The freeze-dried compound was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for inhibition of osteoclast differentiation (Table F).

Table F: Effect of L-Aspartic acid, N-sulphonic acid calcium salt on osteoclast formation

Culture conditions	**Number of TRAP-positive multinuclear cells/well of 96 well plate (Mean ± SEM)**	**% inhibition**
M-CSF	0	-
M-CSF + RANKL	158.33 ± 11.26	0
M-CSF + RANKL + compound 4 (0.5 µg/ml)	127.30 ± 5.50	19.70
M-CSF + RANKL + compound 4 (1.5 µg/ml)	86.23± 7.23	45.16
M-CSF + RANKL + compound 4 (3.0 µg/ml)	44.50± 4.80	71.90
M-CSF + RANKL + compound 4 (5.0 µg/ml)	26.67± 0.73	83.26

For detail see legend to example 5

Reference example 15

L-homoglutamic acid, N-sulphonic acid as prepared in example 4 was mixed with 1 M equivalent of $CaCl_2$ solution and incubated at temperature ranging from 30 ± 5^{o} C. The resulting complex was freeze-dried. The freeze-dried compound was reconstituted in sterilized distilled water and assessed in a dose-dependent manner for inhibition of osteoclast differentiation (Table G).

Table G: Effect of L-homoglutamic acid, N-sulphonic acid, calcium salt on osteoclast formation

Culture conditions	**Number of TRAP-positive multinuclear cells/well of 96 well plate (Mean ± SEM)**	**% inhibition**
M-CSF	0	-
M-CSF + RANKL	146..83 ± 12.00	-
M-CSF + RANKL + compound 2 (0.5 μg/ml)	138.57 ± 7.95	5.55
M-CSF + RANKL + compound 2 (1.5 μg/ml)	106.23 ± 10.47	27.60
M-CSF + RANKL + compound 2 (3.0 μg/ml)	78.57 ± 13.57	46.40
M-CSF + RANKL + compound 2 (5.0 μg/ml)	46.22±10.00	68.50

For detail see legend to example 5

Reference example 16

A. *In vitro* osteoclastogenesis assay

For *in vitro* osteoclastogenesis bone marrow cells were isolated from 5-to 8-wk-old Balb/c mice. Mice were sacrificed by cervical dislocation and femora and tibiae were aseptically removed and dissected free of adherent soft tissues. The bone ends were cut, and the marrow cavity was flushed out with medium MEM from one end of the bone using a sterile 21-gauge needle. The bone marrow suspension was carefully agitated with a plastic Pasteur pipette to obtain a single-cell suspension. The cells were washed twice and resuspended (10^6 cells/ml) in αMEM containing 10% FBS. Stromal cell-free, M-CSF-dependent, osteoclast precursor cells were prepared from these cells as previously described (Wani *et al.* 1999). Briefly, bone marrow cells were incubated

for 24 h in αMEM containing 10% FBS in the presence of M-CSF (10 ng/ml) at a density of 3 x 10^5 cells/ml in a 75 cm^2 flask. After 24 h, nonadherent cells were harvested and layered on a Ficoll-Hypaque gradient. Cells at the gradient interface were collected, washed and resuspended (5 x 10^5/ml) in αMEM containing 10% FBS. In this study, we called these stromal cell-free, M-CSF-dependent, nonadherent cells as osteoclast precursors. These osteoclast precursors were added to 96-well plates (100 µl/well) containing plastic coverslips. Each well received further 100 µl of medium containing M-CSF (30 ng/ml), RANKL (30 ng/ml) without or with various concentrations of purified compound. Cultures were fed every 2-3 days and after incubation for 6 days osteoclast formation was evaluated by tartrate-resistant acid phosphatase (TRAP) staining. The number of TRAP-positive multinucleated cells (MNCs) containing 3 or more nuclei was scored.

Characterization of osteoclasts by TRAP staining

Osteoclast formation was evaluated by quantification of TRAP-positive MNCs as described previously (Khapli *et al.* 2003). TRAP is preferentially expressed at high levels in osteoclast and is considered, especially in the mouse, to be an osteoclast marker. Cytochemical staining for TRAP is widely used for identifying the osteoclasts *in vivo* and *in vitro*. It is claimed to be specific for osteoclasts in bone. After incubation, cells on cover slips were washed in PBS, fixed in 10% formalin for 10 min and stained for acid phosphatase in the presence of 0.05 M sodium tartrate. The substrate used was napthol AS-BI phosphate. Only those cells that were strongly TRAP-positive (dark red) counted by light microscopy.

***In Vitro* Bone resorption assay**

Osteoclast has the ability to excavate authentic resorption lacunae *in vivo* and *in vitro*. Bone resorption is the unique function of the osteoclast and is therefore the most useful means of distinguishing it from other cell types. M-CSF-dependent, non-adherent bone marrow cells were incubated for 10 days on bovine cortical bone slices in the presence of M-CSF, RANKL with or without various concentrations of compounds. Bone slices were examined for resorption pits by reflected light microscopy as previously described (Wani *et al.* 1999).